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NEWS 15	FEB 11	WTEXTILES reloaded and enhanced
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NEWS 20	FEB 23	TOXCENTER updates mirror those of MEDLINE - more precise author group fields and 2009 MeSH terms
NEWS 21	FEB 23	Three million new patent records blast AEROSPACE into STN patent clusters
NEWS 22	FEB 25	USGENE enhanced with patent family and legal status display data from INPADOCDB
NEWS 23	MAR 06	INPADOCDB and INPAFAMDB enhanced with new display formats
NEWS 24	MAR 11	EPFULL backfile enhanced with additional full-text applications and grants

NEWS 25 MAR 11 ESBIOBASE reloaded and enhanced
NEWS 26 MAR 20 CAS databases on STN enhanced with new super role for nanomaterial substances
NEWS 27 MAR 23 CA/CAplus enhanced with more than 250,000 patent equivalents from China

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FILE 'HOME' ENTERED AT 08:43:03 ON 30 MAR 2009

=> file reg
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 0.22 0.22

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DICTIONARY FILE UPDATES: 27 MAR 2009 HIGHEST RN 1128305-29-2

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105309021mm/dd/yyyy>

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chain nodes :
6 7 8 9 11 14
ring nodes :
1 2 3 4 5
chain bonds :
3-14 4-9 5-6 6-7 6-8 9-11
ring bonds :
1-2 1-5 2-3 3-4 4-5
exact/norm bonds :
1-2 1-5 2-3 3-14 9-11
exact bonds :
3-4 4-5 4-9 5-6
normalized bonds :
6-7 6-8
isolated ring systems :
containing 1 :

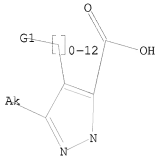
G1:X,Ak

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:CLASS 9:CLASS
11:CLASS 14:CLASS

105309021mm/dd/yyyy>

L1 STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1 STR



G1 X,Ak

Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 08:43:34 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 1264 TO ITERATE

100.0% PROCESSED 1264 ITERATIONS 11 ANSWERS
SEARCH TIME: 00.00.03

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 23148 TO 27412
PROJECTED ANSWERS: 22 TO 418

L2 11 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 08:43:43 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 25921 TO ITERATE

100.0% PROCESSED 25921 ITERATIONS 253 ANSWERS
SEARCH TIME: 00.00.01

L3 253 SEA SSS FUL L1

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COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 185.88 186.10

FILE 'CAPLUS' ENTERED AT 08:43:48 ON 30 MAR 2009
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FILE COVERS 1907 - 30 Mar 2009 VOL 150 ISS 14
FILE LAST UPDATED: 29 Mar 2009 (20090329/ED)

Caplus now includes complete International Patent Classification (IPC)
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This file contains CAS Registry Numbers for easy and accurate
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```
=> s l3
L4          145 L3

=> l4 and HDL
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"HELP COMMANDS" at an arrow prompt (=>).

=> S L4 AND HDL
          30628 HDL
             423 HDLS
          30692 HDL
                (HDL OR HDLS)
L5            1 L4 AND HDL

=> S L4 AND METABOLIC
         261888 METABOLIC
             32 METABOLICS
         261913 METABOLIC
                (METABOLIC OR METABOLICS)
L6            0 L4 AND METABOLIC

=> D L4 IBIB ABS HITSTR 120-145
```
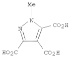
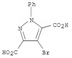

L4 ANSWER 120 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1968:459149 CAPLUS
DOCUMENT NUMBER: 69:59149
ORIGINAL REFERENCE NO.: 69:11055a,11058a
TITLE: The effect of phosphoryl chloride on 1-acetyl-3,5,5-trimethylpyrazoline. A new synthesis of bipyrazoles
AUTHOR(S): Kost, A. N.; Golubeva, G. A.; Sviridova, L. A.; Grandberg, I. I.; Chernyshova, N. B.
CORPORATE SOURCE: Mosk. Gos. Univ. im. Lomonosova, Moscow, USSR
SOURCE: Doklady Akademii Nauk SSSR (1968), 179(2), 337-40
CODEN: DANKAS; ISSN: 0002-3264
DOCUMENT TYPE: Journal
LANGUAGE: Russian
GI For diagram(s), see printed CA Issue.
AB 1-Acetyl-3,5,5-trimethyl-2-pyrazoline reacts exothermically with $POCl_3$ and a mixture of equal wts. of these substances heated 3 hrs. on a steam bath, kept overnight at room temperature, then treated with ice, made alkaline with K_2CO_3 at 0°, and extracted with C_6H_6 gave 85% 3-(3,5,5-trimethyl-2-pyrazolin-1-yl)-5-methylpyrazole (I), m. 100° (octane) (benzoyl derivative m. 107-8°), which heated with S at 230-40° gave H_2S and 75% 3-(3,4,5-trimethyl-1-pyrazolyl)-5-methylpyrazole (II), m. 150°; acetyl derivative m. 121-2°. II oxidized with $KMnO_4$ in H_2O gave 1-methyl-3,4,5-pyrazoletricarboxylic acid, decomposed above 350°; tri-Me ester m. 76-8°.
IT 20544-79-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 20544-79-0 CAPLUS
CN 1H-Pyrazole-3,4,5-tricarboxylic acid, 1-methyl- (CA INDEX NAME)



L4 ANSWER 121 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1968:427955 CAPLUS
DOCUMENT NUMBER: 69:27955
ORIGINAL REFERENCE NO.: 69:5235a,5238a
TITLE: Polypyrazole polyamides
AUTHOR(S): Chiriac, C.; Stoicescu-Crivat, L.; Zugravescu, I.
CORPORATE SOURCE: Inst. Macromol. Chem. "P. Poni", Iasi, Rom.
SOURCE: Revue Roumaine de Chimie (1967), 12(12), 1489-93
CODEN: RRCHAX; ISSN: 0035-3930
DOCUMENT TYPE: Journal
LANGUAGE: French
GI For diagram(s), see printed CA Issue.
AB Several polymers, containing pyrazole and aromatic rings linked by amide groups, were prepared by interfacial polycondensation of the dichloride (I) of 1-phenyl-3,5-pyrazoledicarboxylic acid (II) and that (III) of 1-phenyl-4-bromo-3,5-pyrazoledicarboxylic acid (IV), with ethylenediamine (V), hexamethylenediamine (VI), piperazine (VII), and p-phenylenediamine (VIII). The symmetry of the positions of the reactive groups and the substitution of the H at the pyrazole N favored the stability of the products. To a dilute solution of 10 millimoles V, VI, VII, or VIII in 0.5 l. H_2O containing 20 millimoles NaOH, a solution of 10 millimoles I or III in 0.2 l. $CHCl_3$ was added rapidly while stirring. Maximum mol. weight and maximum yield were attained when the 2 reagents were added very pure and dry, and were brought together in equivalent amts. near the reaction zone, close to the interface. After the fast precipitation of the polymer IX, stirring was continued at ambient temperature for 45 min., and the product was centrifuged, washed (H_2O, $CHCl_3$), and dried in vacuo at 100°. Most IX prepared were white powders [except IX (R = H or Br, R' = p-NHC6H4NH), which were darker]. The properties of the polymers were (R,R', m.p., and inherent viscosity at 20° in a 0.5% solution in m-cresol given): H,NH(CH2)2NH, 255-8°, 0.47; H, NH(CH2)6NH, 239-50°, 0.55; H, 1,4-piperazinediyl, 274-8°, 0.60; H, p-NHC6H4NH, 317-24°, 1.01; Br, NH(CH2)2NH, 256-60°, -; Br, NH(CH2)6NH, 244-9°, 0.68; Br, 1,4-piperazinediyl, 263-9°, 0.85; Br, p-NHC6H4NH, 332-7°, 0.87. The polymers were insol. in customary solvents, and those containing aliphatic units were soluble in HCONMe2, Me2SO, and HCO_2H, whereas those with R' = p-NHC6H4NH dissolved only in m-cresol and H_2SO_4; the solubility decreased with increasing m.p. Heat treatment at 200° under vacuum for 8-10 hrs. did not alter the polymers, as demonstrated by ir spectra. Whereas the aliphatic polymers lost 4-2% at 300°, and the aromatic only 2-1%, IX (R' = NH(CH2)2NH) lost 56-50% at 400°, and IX (R' = p-NHC6H4NH) only 5-4%; the stability of the polymers with R = H was almost the same as those of R = Br. The high values of the inherent viscosity were attributed to the interfacial polycondensation method employed in their preparation The structure of the polymers was confirmed by

L4 ANSWER 121 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN (Continued)
anal. and by the ir spectra, in which the bands characteristic of pyrazoles appeared at 1500-10, and those of CONH at 1640-50 cm.-1. The high thermal stability of these polymers was attributed to the pyrazole ring, which ensured the integrity of the polymer chain at elevated temp. Preliminary tests demonstrated that the polymers contg. methylenic groups in the chain were capable of film and fiber formation. The fibers were formed by melt-spinning; they were transparent, elastic, and resistant. The raw materials in these polycondensations were prepd. as follows: II, m. 266°, by condensation of acetylacetone with PhNHNH2, followed by oxidn. with $KMnO_4$; IV, m. 244° (H_2O), dropwise addn. of 3.2 g. Br while stirring to 4.64 g. II and 3.36 g. anhyd. NaOAc in 90 cc. glacial AcOH, leaving 24 hrs. at room temp., distg., and crystg. HCONMe2, at 84% yield. I and III, m. 95 and 105°, resp., were prepd. by reaction with $SOCl_2$ in HCONMe2, followed by vacuum evapn. and washing with petroleum ether.
IT 20638-31-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 20638-31-7 CAPLUS
CN 1H-Pyrazole-3,5-dicarboxylic acid, 4-bromo-1-phenyl- (CA INDEX NAME)



L4 ANSWER 122 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1968:87293 CAPLUS
DOCUMENT NUMBER: 68:87293
ORIGINAL REFERENCE NO.: 68:16842h,16843a
TITLE: 6-Aminopenicillanic acid derivatives
INVENTOR(S): Feher, Odon; Koczka, Istvan; Vargha, Laszlo
PATENT ASSIGNEE(S): Gyogyszerkutato Intezet
SOURCE: Hung., 17 pp.
CODEN: HUXXAT
DOCUMENT TYPE: Patent
LANGUAGE: Hungarian
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

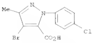
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
HU 153762		19670622	HU	19650924

AB Et3N (3.58 g.) and then a solution of 5.30 g. 1-phenyl-3-methyl-4-bromo-5-pyrazolecarboxylic acid chloride (m. 71-2°) in 60 ml. $CHCl_3$ are added with stirring to a suspension of 7.65 g. 6-aminopenicillanic acid in 250 ml. $CHCl_3$ at 0-3°, the mixture is stirred at 0-3° for 3 hrs., filtered, and extracted with dilute H_3PO_4 and H_2O at 0-3°. The organic phase is dried and a solution of 2.64 g. n-C7H15CO2K in 12 ml. BuOH added to yield 7 g. 1-phenyl-3-methyl-4-bromo-5-pyrazolylpenicillin K salt. The K salts of the following derivs. were prepared analogously (m.p. of the acid chloride used is given): 1-(p-bromophenyl)-3-methyl-4-bromo-5-pyrazolylpenicillin (133-4°); 1-(p-chlorophenyl)-3-methyl-4-bromo-5-pyrazolylpenicillin (128-30°); 1-(p-chlorophenyl)-3-methyl-4-chloro-5-pyrazolylpenicillin (114-15°); 1-cyclohexyl-3-methyl-4-chloro-5-pyrazolylpenicillin (62-4°); 1-phenyl-3,4-dimethyl-5-pyrazolylpenicillin (b. 179-82°); 1-(p-chlorophenyl)-3,4-dimethyl-5-pyrazolylpenicillin (135-7°); 1-phenyl-4-methyl-5-pyrazolylpenicillin (65-7°); 1-(p-chlorophenyl)-4-methyl-5-pyrazolylpenicillin (112-13°); 1-(2,6-dichlorophenyl)-4-methyl-5-pyrazolylpenicillin [K salt monohydrate [α]20D 109.9° (c 1, $CHCl_3$)] (86-8°); 1-(2,4,6-trichlorophenyl)-4-methyl-5-pyrazolylpenicillin (101-2°); and 1-cyclohexyl-4-methyl-5-pyrazolylpenicillin (64-5°). EtO2CCOCH:CMeOEt was treated with p-ClC6H4NHNH2 to yield 1-(p-chlorophenyl)-3-methyl-5-ethoxycarbonylpyrazole, m. 129-30°, which was then hydrolyzed and brominated to give 1-(p-chlorophenyl)-3-methyl-4-bromopyrazole-5-carboxylic acid, m. 224-6° (decomposition). Similarly were obtained: 1-(p-chlorophenyl)-3-methyl-4-chloro-5-ethoxycarbonylpyrazole, m. 126-7°, the acid m. 221-3° (decomposition), and 1-cyclohexyl-3-methyl-4-chloro-5-carboxypyrazole, m. 185-7° (decomposition). 1-(2-Furyl)-2-methyl-1,3-butanedione was condensed with PhNHNH2 to give 1-phenyl-3,4-dimethyl-5-(2-furyl)pyrazole, which was oxidized with $KMnO_4$ to yield 1-phenyl-3,4-dimethyl-5-pyrazolecarboxylic acid, m. 168-71°. Similarly were synthesized: 1-(p-chlorophenyl)-3,4-dimethyl-5-(2-furyl)pyrazole, m. 80-2°, and 1-(p-chlorophenyl)-3,4-dimethyl-5-carboxypyrazole, m. 229-32° (decomposition). Reaction of Et 2-oxobutyrate with HC(OEt)3 in the presence of Ac2O gave Et 2-oxo-3-ethoxymethylenebutyrate, which was condensed with PhNHNH2 to yield 1-phenyl-4-methyl-5-ethoxycarbonylpyrazole, m.

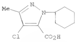
L4 ANSWER 122 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN (Continued)
45-7°; the acid m. 206-8° (decompn.). Similarly were obtained 1-(p-chlorophenyl)-4-methyl-5-ethoxycarbonylpyrazole, m. 80-1°; the acid m. 204-7° (decompn.); 1-(2,6-dichlorophenyl)-4-methyl-5-carboxypyrazole, m. 225-31° (decompn.); 1-(2,4,6-trichlorophenyl)-4-methyl-5-carboxypyrazole, m. 249-53° (decompn.); and 1-cyclohexyl-4-methyl-5-carboxypyrazole, m. 172-4°.

IT 15949-56-1P 15949-60-7P 17703-09-2P 17703-11-6P 17703-12-7P
RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of)

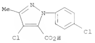
RN 15949-56-1 CAPLUS
CN 1H-Pyrazole-5-carboxylic acid, 4-bromo-1-(4-chlorophenyl)-3-methyl- (CA INDEX NAME)



RN 15949-60-7 CAPLUS
CN 1H-Pyrazole-5-carboxylic acid, 4-chloro-1-cyclohexyl-3-methyl- (CA INDEX NAME)

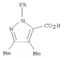


RN 17703-09-2 CAPLUS
CN 1H-Pyrazole-5-carboxylic acid, 4-chloro-1-(4-chlorophenyl)-3-methyl- (CA INDEX NAME)

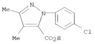


RN 17703-11-6 CAPLUS
CN 1H-Pyrazole-5-carboxylic acid, 3,4-dimethyl-1-phenyl- (CA INDEX NAME)

L4 ANSWER 122 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN (Continued)



RN 17703-12-7 CAPLUS
CN 1H-Pyrazole-5-carboxylic acid, 1-(4-chlorophenyl)-3,4-dimethyl- (CA INDEX NAME)



L4 ANSWER 123 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER:	1967:482208 CAPLUS
DOCUMENT NUMBER:	67:82208
ORIGINAL REFERENCE NO.:	67:15511a,15514a
TITLE:	Derivatives of 6-aminopenicillanic acid
PATENT ASSIGNEE(S):	Chinoin Gyogyszer es Vegyeszeti Termekek Gyara Rt.
SOURCE:	Neth. Appl., 17 pp. CODEN: NAXXAN
DOCUMENT TYPE:	Patent
LANGUAGE:	Dutch
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
NL 6613374		19670328	NL 1966-13374	19660922
AT 268520			AT	
DE 1670382			DE	
FR 5732			FR	
GB 1134808			GB	
US 3376288		19680402	US 1966-553691	19660531
PRIORITY APPLN. INFO.:			HU	19650924

OTHER SOURCE(S): MARPAT 67:82208
GI For diagram(s), see printed CA Issue.

AB The title compds. (I) are prepared by known methods, are active against penicillinase-producing strains of Staphylococcus aureus, are relatively stable against mineral acid, and have a fast resorption rate from the digestive tract. Thus, a mixture of 4.0 g. 1-phenyl-3-methyl-4-bromopyrazole-5-carboxylic acid, 20 ml. C6H6, and 6 ml. SOCl2 is refluxed 1 hr. to yield the corresponding acid chloride (II), m. 71-2° (petroleum ether b. 60-80°). To a mixture of 7.65 g. 6-aminopenicillanic acid (III) in 250 ml. dry CHCl3 is added dropwise with stirring at 0-3° 3.85 g. Et3N; to this mixture is added in 2 hrs. with stirring a solution of 5.3 g. II in 60 ml. dry CHCl3, the mixture stirred 3 hrs. at 0-3°, excess III filtered off, and the solution is worked up to yield 7.0 g. K 1-phenyl-3-methyl-4-bromo-5-pyrazolylpenicillanate (IV), purity 85% (iodometric assay). A mixture of 10 g. 1-carbethoxy-1-oxo-3-ethoxy-2-butene (V), 9.6 g. p-chlorophenylhydrazine-HCl, 4.45 g. anhydrous NaOAc, and 70 ml. anhydrous AcOH is heated 1 hr. at 95-100° to yield 1-(p-chlorophenyl)-3-methyl-5-carbethoxypyrazole (VI), m. 128-30° (50% aqueous EtOH), which is saponified by boiling 1 hr. with 50 ml. 10% KOH in EtOH to yield 1-(p-chlorophenyl)-3-methylpyrazole-5-carboxylic acid (VII), m. 212-14° (decomposition) (EtOH). To a mixture of 2.81 g. VII and 65 ml. AcOH is added 1.9 g. Br and the mixture kept with stirring 1 hr. at 20-5° and 5 min. at 95-100° to yield 4-bromo derivative (VIII) of VII, m. 224-6° (decomposition) (EtOH). VIII is converted with SOCl2 into the acid chloride IX, m. 128-30°. From 1.05 g. III and 0.81 g. IX is obtained (as described for IV) 1.07 g. K 1-(p-chlorophenyl)-3-methyl-4-bromo-5-pyrazolylpenicillanate, purity 78%. A mixture of 8.5 g. VI, 85 ml. dry C6H6, and 5.3 ml. SO2Cl2 is refluxed 1

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hr. to yield 4-chloro deriv. of VI, m. 126-7°, which is converted via 4-chloro deriv. of VII, m. 221-3° (decompn.), into the acid chloride (X), m. 114-15°. From 10.4 g. III and 7.0 g. X is obtained 11.1 g. K 1-(p-chlorophenyl)-3-methyl-4-chloro-5-pyrazolylpenicillanate, purity 95%. From 5.58 g. V and 5.65 g. cyclohexylhydrazine-HCl (Xa) is obtained 1-cyclohexyl-3-methyl-5-carbethoxypyrazole, b0.1 111-13°, which is treated with SO2Cl2 and sapond. to yield 1-cyclohexyl-3-methyl-4-chloropyrazole-5-carboxylic acid (XI), m. 185-7° (decompn.) (50% aq. EtOH). XI is converted into the acid chloride (XII), m. 62-4° (petroleum ether b. 40-60°). From 1.17 g. III and 0.71 g. XII is obtained 0.51 g. K 1-cyclohexyl-3-methyl-4-chloro-5-pyrazolylpenicillanate, purity 95%. A mixt. of 39 g. Et 2-oxobutyrate, 54 g. Et orthoformate, 0.07 g. anhyd. ZnCl2, and 77 ml. dry PhMe is heated 5-6 hrs. (the formed EtOH is distd.; PhMe is added gradually) and distd. to yield a fraction b0.2 80-100°, which is dissolved in 40 ml. anhyd. PhMe and refluxed 45-60 min. in the presence of 0.46 g. p-toluenesulfonic acid. The mixt. is distd. to yield Et 2-oxo-3-ethoxymethylenebutyrate (XIII), b0.2 93-9°. From 37.7 g. XIII and 32.3 g. PhNHNH2.HCl is obtained 1-phenyl-4-methyl-5-carbethoxypyrazole, b0.2 135-40°, which is sapond. to yield 1-phenyl-4-methylpyrazole-5-carboxylic acid (XIV), m. 206-8° (decompn.) (EtOH). From XIV is obtained the acid chloride (XV), m. 67-8°. From 2.33 g. III and 1.19 g. XV is obtained 2 g. K 1-phenyl-4-methyl-5-pyrazolylpenicillanate, purity 92%. A mixt. of 5.2 g. XIII, 5 g. p-chlorophenylhydrazine-HCl, and 39 ml. anhyd. EtOH is refluxed 1 hr., 17 ml. 17% aq. NaOH added, and the mixt. refluxed another hr., and the crude product isolated and refluxed 2 hrs. with a mixt. of 20 ml. EtOH and 0.6 ml. concd. H2SO4 to yield 1-(p-chlorophenyl)-4-methylpyrazole-5-carboxylic acid, m. 204-7° (decompn.) (EtOH), which is converted into the acid chloride (XVI), m. 112-13°. From 1.41 g. III and 0.83 g. XVI is obtained 1.1 g. K 1-(p-chlorophenyl)-4-methyl-5-pyrazolylpenicillanate, purity 91%. Starting with XIII and 2,6-dichlorophenylhydrazine-HCl is obtained 1-(2,6-dichlorophenyl)-4-methylpyrazole-5-carboxylic acid, m. 225-31° (decompn.) (40% aq. EtOH), which is converted into the acid chloride (XVII), m. 86-8° (petroleum ether b. 60-80°). From 6.84 g. III and 4.58 g. XVII is obtained 7.12 g 1-(2,6-dichlorophenyl)-4-methyl-5-pyrazolylpenicillin (XVIII)-H2O K salt [α]20D 109.9° (c, 1% acetone). To a mixt. of 2.16 g. III and 20 ml. H2O is added with stirring at 0-5° N aq. NaOH to pH 7.2. To this mixt. is added with stirring a soln. of 2.9 g. XVII in 30 ml. iso-BuCOMe. The mixt. is stirred 2 hrs. at room temp. and worked up to yield 3.1 g. XVIII Na salt, purity 94%. Similarly is prepd. XVIII (89% pure), and XVIII cyclohexylamine salt (93% pure). Starting with XIII and 2,4,6-trichlorophenylhydrazine-HCl is prepd. 1-(2,4,6-trichlorophenyl)-4-methylpyrazole-5-carboxylic acid, m. 249-53° (decompn.) (65% aq. EtOH), which is converted into the acid chloride (XIX), m. 101-2°. From 1.47 g. III and 1.1 g. XIX is prepd. 1.36 g. K 1-(2,4,6-trichlorophenyl)-4-methyl-5-pyrazolylpenicillanate, purity 87%. Starting with XIII and Xa is obtained 1-cyclohexyl-4-methyl-5-carbethoxypyrazole, b0.2 109-14°, which is converted via the carboxylic acid (no phys. consts. given) into the acid chloride (XX), m. 64-5°. From 1.47 g. III and 0.77 g. XX is

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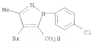
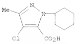
obtained 1.01 g. K 1-(cyclohexyl)-4-methyl-5-pyrazolylpenicillanate, purity 97%. Also claimed is 1-(p-bromophenyl)-3-methyl-4-bromo-5-pyrazolylpenicillin.

IT 15949-56-1P 15949-60-7P 16146-35-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

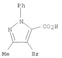
RN 15949-56-1 CAPLUS
CN 1H-Pyrazole-5-carboxylic acid, 4-bromo-1-(4-chlorophenyl)-3-methyl- (CA INDEX NAME)



RN 15949-60-7 CAPLUS
CN 1H-Pyrazole-5-carboxylic acid, 4-chloro-1-cyclohexyl-3-methyl- (CA INDEX NAME)



RN 16146-35-3 CAPLUS
CN 1H-Pyrazole-5-carboxylic acid, 4-bromo-3-methyl-1-phenyl- (CA INDEX NAME)



L4 ANSWER 124 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1966:84541 CAPLUS
DOCUMENT NUMBER: 64:84541
ORIGINAL REFERENCE NO.: 64:15866b-h,15867a-c

TITLE: Azole series. II. 1,3- and 1,5-Dimethylpyrazoles and their brominated derivatives

AUTHOR(S): Elguero, Jose; Jacquier, Robert; Tarrago, Georges; Tien Duc, Hong Cung N.
CORPORATE SOURCE: Ecole Natl. Super. Chim., Fac. Scis., Montpellier

SOURCE: Bulletin de la Societe Chimique de France (1966), (1), 293-302
CODEN: BSCFAS; ISSN: 0037-8968
DOCUMENT TYPE: Journal
LANGUAGE: French

GI For diagram(s), see printed CA Issue.

AB cf. CA 63, 14846d. The structures of 1,3- (I) and 1,5-dimethylpyrazole (II) were established with certainty by synthesis and spectroscopy. The bromination of I and II and some of their derivs. was studied. Na (50 g.) in 1120 cc. absolute EtOH and 270 cc. (CO2Et)2 treated with stirring with 147 cc. dry Me2CO yielded 70% AcCH:C(ONa)CO2Et (III). III (300 g.) in 1750 cc. H2O with 279 g. MeNHNH2.H2SO4 and 90 g. Na2CO3 yielded IV (R = CO2Et) (V), b0.3 77°, and VI (R = CO2Et) (VII), b0.3 129°, in the ratio 1:3. V (13.7 g.) in a little EtOH and 3.6 g. NaOH in H2O refluxed 1.5 hrs. and acidified with HCl gave 86% IV (R = CO2H) (VIII), m. 207°. The decarboxylation of VIII gave I, b44 55°; picrate m. 137.5° (EtOH); HBr salt m. 155° (Et2O). VII (33 g.) refluxed 0.5 hr. with stirring with 8.3 g. NaOH in 30% aqueous NaOH yielded 95% VI (R = CO2H) (IX), m. 174-5° (EtOH). IX decarboxylated yielded 58% II, b25 63-4°; picrate m. 170-1° (EtOH); II.HBr m. 141-3°. AcCH2CHO treated at -60°, with 1 equivalent MeNHNH2, warmed to 25°, and treated with alc. picric acid gave a mixture of the picrates of I and II. MeNHNH2 added dropwise with cooling to AcCH2CH(OMe)2 (X), heated 10 min. on the water bath, diluted with H2O, and heated 20 min. on the water bath with 6N HCl gave 64% bis(methylhydrazone) (XI) of X, b. 140-6°, which with alc. picric acid gave a mixture of about equal parts picrates of I and II, which was also obtained from the crude XI. MeNHNH2 picrate in EtOH and a large excess of X gave the picrates of I and II. 2,4-(O2N)2C6H3F with X in EtOH gave the bis[N-methyl-N-(2,4-dinitrophenyl)hydrazone] of X, m. 187° (CHCl3), which was also obtained from 2,4(O2N)2C6H3NMeNH2 with excess X in EtOH in the presence of a few drops HCl. X treated dropwise at -78° with 1 equivalent MeNHNH2 yielded 90% MeNHN: CMeCH2CH(OMe)2 (XII), b0.05 41-2°. XII with 3N HCl gave I and II. XII (4.5 g.) and 5 cc. H2O treated with 5 cc. 2N AcOH and heated 10 min. on the water bath yielded 32% I, b. 135-40°; picrate m. 137° (EtOH). (MeO)2CHCH2Ac treated 2 hrs. with HC(OMe)3 and a few drops H2SO4 yielded 55% MeC(OMe)2CH2CH(OMe)2 (XIII), b25 90°. XIII treated at - 78° with MeNHNH2 yielded only the picrate of MeNHNH2, m. 165°. MeOCH:CHAc (XIV), b15 75°, m. about 0°, n25D) 1.4634, was

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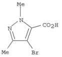
prepd. in 58% yield by the pyrolysis of X. XIV treated with MeNHNH2 at -78° and the crude product with picric acid gave the picrates of I and II. 3(5)-Methyl-5(3)-bromopyrazole (XV) (4 g.) refluxed 1 hr. with 4.7 g. Br yielded quant. 3(5)-methyl-4,5-(3)-dibromopyrazole (XVI), m. 142° (sublimed). XV (16 g.), 15 g. MeI, and 2.4 g. NaOMe in 30 cc. MeOH heated 12 hrs. at 100° in a sealed tube, and the product treated with aq. NaOH, filtered from 1,2,3-trimethyl-5-bromopyrazolium iodide, and extd. with CHCl3 yielded a mixt. of nearly equal parts of IV (R = Br) (XVII) and VI (R = Br). XVI yielded similarly the 4,5-dibromo deriv. (XVIII) of I and the 3,4-dibromo deriv. of II in about equal parts. XVII (8 g.) refluxed 1 hr. with 8 g. Br gave 90% XVIII, m. 69-70° (Et2O-petr. ether). I (10 g.) in AcOH treated dropwise with stirring with 108 cc. Br-AcOH (1 g. 16 cc.) and refluxed 2 hrs. yielded the 4-Br deriv. (XIX) of I, b30 100° picrate m. 177° (EtOH); picrolonate m. 136° (EtOH); XIX.HBr m. 197°. 1,5-Dimethylpyrazole in AcOH with Br gave 70% 4-Br deriv. (XX) of II, b21 105°, m. 40-2°; picrate m. 122-3° (EtOH); picrolonate m. 124° (EtOH); XX.HBr m. 120-2°. VIII refluxed with BrAcOH gave the 4-Br deriv. of VIII, m. 232° (aq. Me2CO). V (1 g.) in CHCl3 treated with cooling with 6 cc. Br-CHCl3contg. 1 g. Br, and refluxed 24 hrs. gave the 4-Br deriv. of V, b2 114°. Similarly were prepd. the 4-Br deriv. of VII, b0.9 151°, and the 4-Br deriv. of IX, m. 194-5° (95% EtOH). AcCH2CO2Et (65 g.) in 130 cc. H2O refluxed 15 min. with 27 cc. N2H4.H2O in 100 cc. H2O gave 75% 3-methylpyrazolone (XXI), m. 215° (EtOH). XXI (10 g.) and 33 g. POBr3 heated 12 hrs. at 180° in a sealed tube gave 85% XV, m. 138-9° (sublimed). AcCH2CO2Et (0.2 mole) and 0.2 mole MeNHNH2 in H2O heated during 0.5 hr. to 70° yielded 50% 1,3-dimethyl-5-pyrazolone (XXII), m. 117° (sublimed). A similar run at 100° yielded 1,3,4-trimethyl-6-oxo-pyrano[5,6-d]pyrazole, m. 167-8° (MePh). XXII and POBr3 heated 12 hrs. at 120° in a sealed tube gave XVII, b30 90°, and XV, m. 138° (sublimed). XXI (10 g.) and 2.3 g. Na in MeOH refluxed 6 hrs. with 18.6 g. p-MeC6H4SO3Me gave 1,5-dimethyl-3-pyrazolone which could not be brominated with POBr3. XV brominated in the presence of Fe yielded 8% XVI, m. 143-5° (sublimed). XIX (5 g.) in 60 cc. HNO3 treated 12 hrs. with 2 cc. Br, and the product chromatographed on Al2O3 yielded XVIII, m. 73°, which was also obtained by the degradation of the Ag salt of 4-bromo-1,3-dimethylpyrazole-5-carboxylic acid with Br. XX (5 g.) in 100 cc. HNO3 refluxed 24 hrs. with 1.6 cc. Br yielded the 3,4-dibromo deriv. (XXIII) of II, b0.05 110°, m. 60°. MeNHNH2.H2SO4 (30 g.) and 60 g. AcONa in the min. amt. H2O treated 3 hrs. with 14.6 g. MeCH:CHCHO in a little AcOH yielded 28% 1,5-dimethylpyrazoline (XXIV), b. 122°; picrate m. 112-13° (EtOH). XXIV (1 mole) in CHCl3 treated slowly with cooling and stirring with 3 moles Br in CHCl3 and refluxed 2 hrs., and the sublimed crude product extd. in a Soxhlet app. with Et2O-petr ether gave the sol. XXIIl, m. 60°, and an unidentified, insol. solid, m.p. varying between 165 and 182°. The ir spectra of 1 and Il are recorded.

IT 5775-88-2P, Pyrazole-5-carboxylic acid, 4-bromo-1,3-dimethyl-
RL: PREP (Preparation)
(preparation of)

RN 5775-88-2 CAPLUS
CN 1H-Pyrazole-5-carboxylic acid, 4-bromo-1,3-dimethyl- (CA INDEX NAME)

L4 ANSWER 124 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN (Continued)



L4 ANSWER 125 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1965:3060 CAPLUS
DOCUMENT NUMBER: 62:3060
ORIGINAL REFERENCE NO.: 62:543g-h,544a-g
TITLE: Reaction of tetraphenylcyclopentadienone with diazomethane
AUTHOR(S): Eistert, Bernd; Langbein, Adolf
CORPORATE SOURCE: Univ. Saarlandes, Saarbruecken, Germany
SOURCE: Justus Liebigs Annalen der Chemie (1964), 678, 78-94
CODEN: JLACBF; ISSN: 0075-4617
DOCUMENT TYPE: Journal
LANGUAGE: German
OTHER SOURCE(S): CASREACT 62:3060
GI For diagram(s), see printed CA Issue.
AB Tetraphenylcyclopentadienone (I) in C6H6 with CH2N2-Et2O in the presence of MeOH gave II as the main product. The same reactants in the absence of OH-containing compds. yielded III by addition to 1 C:C bond in the dark, which can isomerize to IV; in light, the isomeric V is also formed. III was converted with the elimination of N into VI which was successively reduced to VII and aromatized to 1,2,3,5-Ph4C6H2 (VIII). VI was aromatized to 2,3,4,6-Ph4C6HOH (IX). II and III with concentrated mineral acids yielded 2,3,5,6-Ph4C6HOH (X), which was oxidized to tetraphenyl-p-benzoquinone (XI), which also was formed from IX with HNO3 by a Ph migration. (PhCH2)2CO with Bz2 in alc. KOH gave 91-6% I, m. 218°. I (7.7 g.) in 230 cc. dry C6H6 and 230 cc. absolute MeOH treated with 230 cc. 0.6M CH2N2-Et2O (undistd.) or 310 cc. 0.45M CH2N2-Et2O (distilled) and kept 0.5-1 hr. in diffuse daylight gave 5.2 g. II, m. 228-9° (1:1 C6H6-EtOH or ligroine, b. 100-60°). I (4.8 g.) in 150 cc. C6H6 treated 17-20 hrs. in the dark with 200 cc. distilled CH2N2-Et2O yielded 3.9-4.3 g. III, m. 148° (decomposition) (MeOH or EtOH). A similar run with undistd. CH2N2-Et2O gave III and IV. I (9.6 g.) in 300 cc. C6H6 and 250 cc. distilled CH2N2-Et2O irradiated 4-5 hrs. with a 125-w. uv lamp gave about 6.6 g. III-IV mixture which fractionally crystallized from EtOH yielded about 0.05 g. III, m. 148°, 0.5 g. IV, m. 155°, and 1 g. V, m. 208-9° (AcOH, EtOH, or aqueous C5H5N) (chromatographed on silica gel). V was recovered unchanged by treatment with concentrated H2SO4 or by refluxing 3 hrs. with KOH-MeOH. V (0.5 g.) in 10 cc. AcCl refluxed 1 hr., cooled, treated with 10 cc. 70% AcOH, and boiled briefly gave about 0.4 g. N-Ac derivative of V, m. 278° (EtOH). II (2.4 g.) and 3.9 g. HCl in 50 cc. AcOH refluxed 10 min. yielded about 1 g. 1-hydroxy-1-chloromethyl-2,3,4,5-tetraphenyl-2,4-cyclopentadiene (XII), m. 191-2° (petr. ether or 80% PrOH). II (2.4 g.) in 200 cc. dry HCl-Et2O refrigerated 24-30 hrs. gave about 1 g. XII, m. 191-2°. III (2 g.) added in small portions to 25 cc. refluxing C5H5N and refluxed 0.5 hr. yielded 2 g. III.C5H5N, m. 89-91°. III.C5H5N crystallized from

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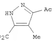
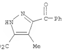
hot petr. ether or 70% MeOH gave 1.65 g. IV, m. 153-4°. III (1 g.) in 3 cc. alc. KOH heated a few min. on a water bath gave 0.6 g. IV, m. 155° (70% MeOH). III (1 g.) and 20 cc. HCl-Et2O kept 24 hrs. at 0° yielded 0.5 g. IV. III (0.3 g.) in 10 cc. AcOH refluxed 1 hr. yielded 0.2 g. IV, m. 156°. III (1 g.) refluxed 2 hrs. with 10 g. AcCl yielded 0.8 g. N-Ac deriv. (XIII) of IV, m. 236° (AcOH). IV (1 g.) gave similarly 0.5 g. XIII. III (21.3 g.) in 500 cc. EtOH treated gradually with 100 cc. concd. HCl and refluxed 4 hrs. gave 11.8 g. X, m. 265° (AcOH). IV (2 g.) gave similarly 1.1 g. X. V (0.5 g.) refluxed 0.5 hr. at about 320° gave a small amt. X. X (0.5 g.), 50 cc. Ac2O, and a few drops concd. H2SO4 heated 20 min. at 100° gave 0.4 g. Ac deriv., m. 252° (AcOH). X (0.5 g.) in 10 cc. BzCl heated 1 hr. at 100° yielded 0.7 g. Bz deriv., m. 269° (AcOH). X(0.5 g.) in 50 cc. C6H6 treated with 25 cc. undistd. CH2N2-Et2O and a few drops MeOH during 24 hrs. yielded nearly quant. the Me ether, m. 226° (AcOH). X (4.0 g.) with Br-CCl4 gave 2.2 g. 4-Br deriv., m. 328-30°. III (3 g.) added in small portions to 25 cc. hot o-xylene and refluxed 15 min. gave 2.2 g. VI, m. 161° (MeOH, EtOH, or petr. ether); red 2,4-dinitrophenylhydrazone m. 235-6° (AcOH). VI (1.5 g.) in 150 cc. C6H6 stirred at room temp. with 0.3 g. LiAlH4 in 100 cc. dry Et2O yielded 1.4 g. VII, m. 198° (petr. ether). VII (1.4 g.) in 100 cc. C6H6 refluxed 1 hr. with 2 g. P2O5 gave 1.1 g. VIII, m. 220°. III (21 g.) added in small portions to refluxing tetrahydronaphthalene (THN), b. 208°, and refluxed 1 hr. yielded 18.8 g. IX, m. 244-5° (AcOH). IV (1 g.) in 15 cc. THN refluxed 10 hrs. gave 0.64 g. IX. V (0.1 g.) refluxed 0.5 hr. at about 315° gave IX. VI (0.1 g.) refluxed 0.5 hr. with 5 cc. THN or warmed with 5 cc. HCl-MeOH or concd. H2SO4, or refluxed several days with AcOH gave IX. IX heated with Ac2O yielded the Ac deriv., m. 181° (AcOH); IX gave with BzCl the Bz deriv., m. 200° (AcOH). IX (1 g.) and 1 g. NaOH in 50 cc. EtOH treated dropwise with stirring with 2 g. Me2SO4 gave 0.85 g. Me ether, m. 177-8°. IX in C6H6 shaken with aq. alk. K3Fe(CN)6 gave a soln. of the red paramagnetic 2,3,4,6-Ph4C6HO• radical which is stable towards O. p-BrC6Ph4OH (0.85 g.) in 150 cc. AcOH and 10 cc. H2O treated with 0.13 g. CrO3 in 50 cc. AcOH and 5 cc. H2O and heated 0.5 hr. at 60° yielded 0.4 g. orange-red XI, m. 308-10°. Powd. X (5 g.) in 50 cc. concd. HNO3 (d. 1.38) kept 6-10 days at room temp. yielded 2 g. XI, m. 308° (70% AcOH). XI (1 g.) in 150 cc. AcOH with about 1 g. Zn dust gave 0.5 g. p-Ph4C6(OH)2, m. 311-13° (AcOH); diacetate m. 318° (AcOH). The reaction of I with CH2N2 was followed by thin-layer chromatography on silica gel; the chromatograms are recorded. The infrared spectra of II-VI are recorded.
IT 877-00-9 888-08-4
(Derived from data in the 7th Collective Formula Index (1962-1966))
RN 877-00-9 CAPLUS
CN 1H-Pyrazole-5-carboxylic acid, 3-acetyl-4-methyl- (CA INDEX NAME)

L4 ANSWER 125 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN (Continued)



RN 888-08-4 CAPLUS
CN 1H-Pyrazole-5-carboxylic acid, 3-benzoyl-4-methyl- (CA INDEX NAME)



L4 ANSWER 126 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1965:3059 CAPLUS
DOCUMENT NUMBER: 62:3059
ORIGINAL REFERENCE NO.: 62:543b-g
TITLE: Bicyclic dilactams
AUTHOR(S): Birkofer, Leonhard; Feldmann, Horst
CORPORATE SOURCE: Univ. Cologne, Germany
SOURCE: Justus Liebigs Annalen der Chemie (1964), 677, 154-6
CODEN: JLACBF; ISSN: 0075-4617
DOCUMENT TYPE: Journal
LANGUAGE: German
OTHER SOURCE(S): CASREACT 62:3059
GI For diagram(s), see printed CA Issue.
AB α,β-Unsatd. dicarboxylic acid esters added CH2N2 and N2CHCO2Me (I) to form carbalkoxy-2-pyrazolinecarboxylic acid esters. On catalytic hydrogenation, these were initially converted by ring opening into diaminodicarboxylic acid esters, which condensed to bicyclic lactams, which were hydrolyzed by aqueous Ba(OH)2, to the corresponding diaminodicarboxylic acids. To Et2O-CH2N2 (from 40 g. H2NCONMeNO) was added dropwise 20 g. di-Me glutaconate (Ia) in 50 cc. Et2O with cooling and the solution kept 2 days, treated with some AcOH to decompose unused CH2N2, and evaporated to give II, oil which crystallized after several days, m. 106°. (II) (R = Me, R1 = R2 = H, n = 1); (III) (R = Me, R1 = CO2Me, R2 = H, n = 1); (IV) (R = Et, R1 = R2 = H, n = 2); (V) (R = Me, R1 = H, R2 = CO2Me, n = 1); From tri-Me aconitate and di-Et 1-butene-1,4-dicarboxylate were similarly prepared III and IV, resp., pale yellow oils, which exploded violently on attempted distillation Ia (20 g.) and 6.6 g. I heated 72 hrs. at .apprx.80° and some unchanged I removed in vacuo from the resulting oil gave V, viscous oil. The following was the general procedure for preparation of dilactams. Crude II-V (20-g. amts.) in 200 cc. EtOH hydrogenated over Raney Ni 6 hrs. at 60° and 120-30 atmospheric, the solution filtered and evaporated, and the residue triturated with 200 cc. dry Me2CO gave 8.5 g. VI, m. 252° (decomposition) (H2O-MeOH); 12 g. VII, m. 110° (MeOH); 7 g. VIII, m. 202° (decomposition) (H2O-EtOH); and 9 g. IX, m. 152° (H2O-MeOH), resp. VI-VIII (2-g. amts.) refluxed 5 hrs. with 100 cc. H2O containing 6 g. Ba(OH)2.8H2O, excess Ba2+ ions precipitated with H2SO4, and the solution filtered, concentrated, and diluted with 30 cc. absolute EtOH gave the following diaminodicarboxylic acids (70-80% yields; oils which crystallized on prolonged standing or after repeated brief boiling with some aqueous alc.): HO2C(CH2)nCR(CH2NH2)CH(NH2)CO2H (X) (R = H, n = 1), m. 201° (decomposition), violet ninhydrin reaction; X (R = CO2H, n = 1), 1 form m. 212° (decomposition), brown violet ninhydrin reaction, and another form m. 240° (decomposition); and X (R = H, n = 2), m. 200° (decomposition), violet ninhydrin reaction, resp. (VI) (R = R1 = H); (VII) (R = CO2Me, R1 = H); (IX) (R = H, R1 = CO2Me); To 2 g. LiAlH4 suspended in 250 cc. dry tetrahydrofuran was added 1.5 g. VI with stirring, the mixture refluxed 8 hrs., treated with 15 cc. H2O, stirred 2 hrs. and filtered, and the filtrate dried and evaporated in vacuo to give 0.7 g. 2,7-diazabicyclo[3.3.0]octane, oil; 84% dioxalate m. 191°

L4 ANSWER 126 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN (Continued)
(decomp.) (ECOH).
IT 877-00-9 888-08-4
(Derived from data in the 7th Collective Formula Index (1962-1966))
RN 877-00-9 CAPLUS
CN 1H-Pyrazole-5-carboxylic acid, 3-acetyl-4-methyl- (CA INDEX NAME)

RN 888-08-4 CAPLUS
CN 1H-Pyrazole-5-carboxylic acid, 3-benzoyl-4-methyl- (CA INDEX NAME)

L4 ANSWER 127 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1961:137440 CAPLUS
DOCUMENT NUMBER: 55:137440
ORIGINAL REFERENCE NO.: 55:25921-h
TITLE: The orientation of some bromo-1-phenylpyrazoles
AUTHOR(S): Finar, I. L.; Miller, D. R.
CORPORATE SOURCE: Northern Polytech., London
SOURCE: Journal of the Chemical Society (1961) 2769-72
CODEN: JCSOAR; ISSN: 0368-1769
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Bromination of 7-methyl-1-phenylpyrazole (I) gave 4-bromo-3-methyl-1-phenylpyrazole (II), which brominated further to 4-bromo-3-methyl-1-(p-bromophenyl)pyrazole (III), m. 98°, and not to the 4,5-Br2 derivative of I as suggested by Michaelis and Behn (Ber. 33, 2595(1900)). Nitration of 0.04 mole II in 45 cc. H2SO4 (d. 1.54) by dropwise addition of 35 cc. concentrated H2SO4 and 35 cc. HNO3 (d. 1.42) at 75° 0.5 hr. then at 12° 0.5 hr. and pouring on ice gave after crystallization from MeOCO 93% 4-bromo-3-methyl-1-(p-nitrophenyl)pyrazole (IV), m. 200-1°. IV was reduced by refluxing 1 hr. in EtOH with 5% Pd-C and 60% aqueous N2H4 to 72% amine (V), m. 96-8°; Ac derivative m. 210.5-11.5°. A Sandmeyer reaction with V gave III. Similarly, 5-carboxy-3-methyl-1-phenylpyrazole (VI) brominated first to the 4-Br derivative (VII) then (but only when the Na salt was used) to 4-bromo-5-carboxy-3-methyl-1-(p-bromophenyl)-pyrazole (VIII). VI Ag salt gave with Br the 4,5-Br2 derivative (IX) of I. IX nitrated to the p-nitrophenyl derivative (m. 162.5-3°, 90%) and reduced to the amine [HCl salt m. 262-3° (decomposition)] gave by a Sandmeyer reaction the same 4,5-dibromo-3-methyl-1-(p-bromophenyl)pyrazole as obtained by Br on the Ag salt of VIII. Decarboxylation of VIII gave III.
IT 16146-35-9P, Pyrazole-5-carboxylic acid, 4-bromo-1-methyl-3-phenyl- 99967-33-1P, Pyrazole-5-carboxylic acid, 4-bromo-1-(p-bromophenyl)-3-methyl-
RL: PREP (Preparation)
(preparation of)
RN 16146-35-9 CAPLUS
CN 1H-Pyrazole-5-carboxylic acid, 4-bromo-3-methyl-1-phenyl- (CA INDEX NAME)

RN 99967-33-1 CAPLUS
CN 1H-Pyrazole-5-carboxylic acid, 4-bromo-1-(4-bromophenyl)-3-methyl- (CA

L4 ANSWER 127 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN (Continued)
INDEX NAME)

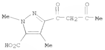
L4 ANSWER 128 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1958:113645 CAPLUS
DOCUMENT NUMBER: 52:113645
ORIGINAL REFERENCE NO.: 52:20133a-h
TITLE: Bipyrazolyls from C-acetylpyrazoles
AUTHOR(S): Brain, E. G.; Finar, I. L.
CORPORATE SOURCE: Northern Polytech., London
SOURCE: Journal of the Chemical Society (1958) 2486-9
CODEN: JCSOAR; ISSN: 0368-1769
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB 3-Acetylpyrazoles have been converted into pyrazolyl-substituted β-diketones and benzylideneacetylpyrazoles, both of which have been used to prepare substituted bipyrazolyls. To a refluxing mixture of NaOEt (from 3.4 g. Na) in 300 cc. EtOH and 80 cc. EtOAc was added 15.6 g. Et 3-acetyl-1,4-dimethylpyrazole-5-carboxylate and refluxing continued 3 hr., then 2 moles MeOEt added, and refluxing continued another 3 hrs. The mixture was extracted with H2O and N NaOH to give 39% 3-acetoacetyl-1,4-dimethylpyrazole-5-carboxylic acid (I), m. 179-80° (CSH6 containing 5% EtOH). By the same method was prepared 32% Et 3-benzoylacetyl-1,4-dimethylpyrazole-5-carboxylate (II), m. 109° (ligroine). Claisen condensation of Et 5-acetyl-4-methylpyrazole-3-carboxylate and EtOAc gave 28% Et 3-acetoacetyl-4-methylpyrazole-5-carboxylate (III), m. 123-4° (CSH6). A mixture of 1 mole I, 1.1 moles 60% (NH2)2.H2O, and 30 cc. EtOH heated 30 min. on a steam bath, H2O added, and the solution cooled gave brown crystals which when twice recrystd. from H2O yielded pure 1,3',4-trimethyl-3,5'-bipyrazolyl-5-carboxylic acid, m. 247-8° (decomposition). I (1 mole) condensed with 2 moles PhNHNH2 in refluxing HOAc gave 1.1 g. 1,3',4-trimethyl-1'-phenyl-3,5'-bipyrazolyl-5-carboxylic acid (IV), m. 212-13° (CSH6-ligroine, then dilute EtOH). This acid was brominated in CHCl3 solution to the 4'-bromo derivative, m. 201.5-2.5° (hot dilute EtOH). III condensed with PhNHNH2 gave an oil which was saponified with ethanolic KOH to yield 3',4-dimethyl-1'-phenyl-3,5'-bipyrazolyl-5-carboxylic acid, m. 190-1° (dilute EtOH, then EtOH). This treated with MeSO4 and NaOH in aqueous solution at 90° gave a mixture of 1,3',4-trimethyl-1'-phenyl-5,5'-bipyrazolyl-3-carboxylic acid, m. 232.5-3° (CSH6) and IV. When II was condensed with PhNHNH2 followed by saponification, 2 products resulted: 53% 1,4-dimethyl-1',3'-diphenyl-3,5'-bipyrazolyl-5-carboxylic acid, m. 193-4° (CSH6 containing 10% ligroine), and 8.4% 1,4-dimethyl-1',5'-diphenyl-3,3-bipyrazolyl-5-carboxylic acid, m. 256-6.5° (EtOH). A mixture of 2.0 g. Et 3-acetyl-1,4-dimethylpyrazole-5-carboxylate, 1.06 g. EtSH, 20 cc. 10% aqueous NaOH, and 50 cc. EtOH was allowed to stand 20 hrs., then acidified giving 1.7 g. benzylideneacetyldimethylpyrazolecarboxylic acid (V), m. 267-8° (decomposition) (EtOH); Me ester, m. 177-8° (EtOH). V heated at 280° for 25 min. gave 63% 3-benzylideneacetyl-1,4-dimethylpyrazole, m. 92.5-3.5° (ligroine), which on condensation with PhNHNH2 gave 50% 1,2-dihydro-1',4'-dimethyl-1,5-diphenyl-3,3'-bipyrazolyl, m. 141-2° (ligroine). Oxidation of the latter by KMnO4 in MeCO2 gave 1,4-dimethyl-1',5'-diphenyl-3,3'-bipyrazolyl, m. 179-81° (ligroine). Me 3-benzylideneacetyl-1,4-dimethylpyrazole-5-carboxylate

L4 ANSWER 128 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN (Continued)
refluxed with PhNHNH2 8 hrs. formed Me 4,5-dihydro-1,4-dimethyl-1',5'-diphenyl-3,3'-bipyrazolyl-5- carboxylate, m. 174-5° (EtOH), which was oxidized (KMnO4 in pyridine) to Me 1,4-dimethyl-1',5'-diphenyl-3,3'-bipyrazolyl-5-carboxylate, m. 128-9°, hydrolyzed to the acid, m. 255-6° (decompn.) (EtOH).
Et 5-acetyl-4-methylpyrazole-3-carboxylate was allowed to react with BzH 1.5 days to yield 5-benzylideneacetyl-4-methylpyrazole-3-carboxylic acid, m. 231.5-3° (HOAc), which was condensed with PhNHNH2 and the crude product oxidized (KMnO4-pyridine) to give 4'-methyl-1,5-diphenyl-3,3'-bipyrazolyl-5'-carboxylic acid, m. 273.5-74° (decompn.) (HOAc).

IT 99068-98-1P, Pyrazole-5-carboxylic acid, 3-acetoacetyl-1,4-dimethyl- 106596-01-4P, Pyrazole-5-carboxylic acid, 3-cinnamoyl-1,4-dimethyl-
RL: PREP (Preparation)
(preparation of)

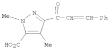
RN 99068-98-1 CAPLUS

CN 1H-Pyrazole-5-carboxylic acid, 3-(1,3-dioxobutyl)-1,4-dimethyl- (CA INDEX NAME)



RN 106596-01-4 CAPLUS

CN 1H-Pyrazole-5-carboxylic acid, 1,4-dimethyl-3-(1-oxo-3-phenyl-2-propen-1-yl)- (CA INDEX NAME)



L4 ANSWER 129 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1958:92839 CAPLUS
DOCUMENT NUMBER: 52:92839
ORIGINAL REFERENCE NO.: 52:16339a-g
TITLE: Research on the structure of glutinic acid. I. Heterocyclic derivatives of the allenic acids
AUTHOR(S): Corsano, Stefano; Capito, Luciana; Bonamico, Mario
CORPORATE SOURCE: Univ. Rome
SOURCE: Annali di Chimica (Rome, Italy) (1958), 48, 140-55
CODEN: ANCRAI; ISSN: 0003-4592
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

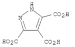
AB The structure of glutinic acid (I), HO2CCH:C:CHCO2H (cf. Jones, C.A. 49, 11556i) is confirmed by ozonolysis; reactions of I with CH2N2, N2CHCO2Et, and PhNHNH2 are studied. A solution of 0.1 g. I in 5 cc. AcOH is ozonized for 1.5 hrs. at 10°, and the effluent gases are passed into Ba(OH)2 (CO2 is evolved). The solution is held under vacuum at room temperature for 1 hr., then HO2CCHO (88% yield) is precipitated as the 2,4-dinitrophenylhydrazone, m. 193-4° (decomposition). A solution of 5 g. I in 50 cc. dry Et2O treated with 6 g. CH2N2 in Et2O then aged overnight in ice ppts. 5 g. Me 3-carbomethoxpyrazole-4-acetate (II), m. 139.5-40.5° (sublimes 130° in high vacuum), also prepared from Me glutinate. Similarly 2.8 g. Me glutaconate is treated with CH2N2, aged overnight, excess destroyed with AcOH, and solution evaporated to give 2.55 g. Me 3-carbomethoxypyrazoline-4-acetate (unstable), which is oxidized by Br-Et2O to II. II (3.7 g.) is hydrolyzed by 3 hrs. refluxing with 20% KOH to 2.6 g. 3-carboxypyrazole-4-acetic acid, m. 241-3° (decomposition). Oxidation of 0.7 g. of this in excess boiling Na2CO3 solution by 2 g. KMnO4, acidification of the hot filtered solution by HNO3 (d. 1.40), and chilling, ppts. 0.32 g. pyrazole-3,4-dicarboxylic acid, m. 255°; di-Me ester, m. 139-41°. A mixture of 3.7 g. Me glutinate and 2.7 g. N2CHCO2Et is heated slowly to 70°, kept there 2 hrs. then overnight at 0°, and the product (5.5 g.) crystallized from aqueous EtOH to give Me 3-carbomethoxy-5-carbethoxypyrazole-4-acetate, m. 109-10° hydrolyzed by 3 hrs. boiling with concentrated HCl to 3,5-dicarboxypyrazole-4-acetic acid (III), m. 234-5° (decomposition). Oxidation of 0.1 g. III in 10 cc. boiling 10% NaOH by KMnO4 (5 hrs.) gives pyrazole-3,4,5-tricarboxylicacid, m. 225-7° isolated by acidification with HNO3, evaporation in vacuo, extraction with Me2CO, evaporation, and crystallization of the residue from dilute HCl. III (1.4 g.) is heated in a retort at 250° till gassing stops, then with a free flame to distil 0.1 g. 4-methylpyrazole, b27 125° (bath temperature); picrate, m. 141-3°. Oxidation of this by aqueous KMnO4 gives pyrazole-4-carboxylic acid, m. 270-5° (decomposition). Me glutinate (0.33 g.) is added to a hot solution of 0.2 g. PhNHNH2 in 30 cc. ligroine (b. 70-80°), and the solution

L4 ANSWER 129 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN (Continued)
refluxed for 1 hr., then the oil is decanted and the soln. cooled several hrs. to ppt. 0.2 g. Me 1-phenyl-5-pyrazolone-3-acetate m. 92-3°, intense red with FeCl3, sol. in 2N HCl, NaOH or Na2CO3. It is hydrolyzed by 30 min. refluxing with 10% KOH to 1-phenyl-5-pyrazolone-3-acetic acid (IV), m. 130-2°. The oil decanted is dissolved in Et2O, and the soln. dild. with ligroine to ppt. 0.05 g. Me 1-phenyl-3-pyrazolone-5-acetate, m. 149-50°, which gives a less intense FeCl3 color. This is hydrolyzed by 6 hrs. refluxing with N NaOH to 1-phenyl-3-pyrazolone-5-acetic acid (V), m. 180° (decompn.). V is heated at 190° till gassing stops, cooled, and the product sublimed at 120°/ 0.5 mm. to give 1-phenyl-5-methyl-3-pyrazolone, m.167-8°. IV and V may be sepd. by paper chromatography in 80:5:15 EtOH-NH4OH-H2O. IV is detected by spraying with diazosulfanilic acid, V only after further spraying with dil. Na2CO3.

IT 19551-66-7P, Pyrazole-3,4,5-tricarboxylic acid
100517-19-9P, Pyrazole-3,5-dicarboxylic acid, 4-(carboxymethyl)-
RL: PREP (Preparation)
(preparation of)

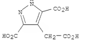
RN 19551-66-7 CAPLUS

CN 1H-Pyrazole-3,4,5-tricarboxylic acid (CA INDEX NAME)



RN 100517-19-9 CAPLUS

CN 1H-Pyrazole-3,5-dicarboxylic acid, 4-(carboxymethyl)- (CA INDEX NAME)



L4 ANSWER 130 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1957:81404 CAPLUS
DOCUMENT NUMBER: 51:81404
ORIGINAL REFERENCE NO.: 51:14694a-g
TITLE: Preparation and properties of some pyrazolylacetic acids
AUTHOR(S): Brain, E. G.; Finar, I. L.
CORPORATE SOURCE: Northern Polytech., London
SOURCE: Journal of the Chemical Society (1957) 2356-9
CODEN: JCSOA9; ISSN: 0368-1769
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB Some pyrazoles containing the AcOH side chain were prepared by means of the Willgerodt reaction, and their activity in the wheat cylinder test was investigated. Et 3-acetyl-4-methylpyrazole-5-carboxylate (I) (19.6 g.) methylated and hydrolyzed gave 17.5 g. crude product which refluxed 3 hrs. with 500 g. 1% MeOH-HCl gave 14.5 g. 3-acetyl-1,4-dimethylpyrazole-5-carboxylic acid (II). The ethereal layer evaporated and the residue hydrolyzed gave 3 g. acid which refluxed 3 hrs. with 1% MeOH-HCl and the unchanged II separated from the Me ester by the above process gave 1.4 g. I Me ester, m. 157-8°. II (14.5 g.) refluxed 3 hrs. with 1% MeOH-HCl gave 11 g. unchanged II, m. 189-91°; Me ester, needles, m. 110-11°. II Et ester (5 g., m. 85-6°), 1.1 g. S, and 7 cc. morpholine refluxed 1 hr. at 150° gave 3.72 g. 5-ethoxycarbonyl-1,4-dimethyl-3-pyrazolyl(thioacetomorpholide) (III), needles, m. 103-4°, or rhombs or platelets, m. 107-8°. Suspensions of these two forms of III in Nujol had different infrared absorption spectra but in CCl4 the spectra were identical. III (5 g.) refluxed 5 hrs. with 75 cc. 10% alc.-KOH gave 2.6 g. 5-carboxy-1,4-dimethyl-3-pyrazolylacetic acid (IV), needles, m. 197°. I similarly treated with S and morpholine gave a noncryst. product and hydrolysis failed to give a solid product. Treatment of the product from 4 g. I with 10-15 cc. concentrated HCl gave 3-ethoxycarbonyl-4-methyl-3-pyrazolyl-(thioacetomorpholide)-HCl (V), crystals, m. 160-1° (from CHCl3-C6H6). V (1 g.) refluxed 3 hrs. with 3N NaOH gave 5-carboxy-4-methyl-3-pyrazolylacetic acid (VI), m. 265-7° (from H2O). The Willgerodt reaction on 5-acetyl-4-methylpyrazole-3-carboxylic acid (4.2 g.) gave a resin, a solution of which in H2O acidified with dilute HCl gave 5-carboxy-4-methyl-3-pyrazolyl(thioacetomorpholide) (VII), yellow precipitate, m. 235-6° (decomposition) (purified by solution in aqueous NaHCO3 and precipitation with HCl). V11 (3 g.) hydrolyzed as above gave 1.9 g. VI. II (15 g.) heated at 240° until vigorous ebullition ceased and the product distilled at 63-5°/0.1 mm. gave 8.7 g. 3-acetyl-1,4-dimethylpyrazole, m. 19-20°. 1V (1.55 g.) refluxed 3 hrs. with 1% MeOH-HCl gave 1.5 g. Me 5-carboxy-1,4-dimethylpyrazole-3-acetate (V1I1), m. 141-2°. VIII (2 g.) heated 1 hr. at 200-40° gave 1.1 g. Me 1,4-dimethyl-3-pyrazolylacetate (IX), b0.05-0.08 76-8°. IX (1 g.) saponified with alc. KOH gave 0.45 g. 1,4-dimethyl-3-pyrazolylacetic acid, m. 107-9° (from C6H6). Crude 4-methyl-3-acetylpyrazole (6.75 g.) similarly subjected to the Willgerodt reaction, but after the reaction,

L4 ANSWER 130 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN (Continued)
excess morpholine removed at 120-30° in vacuo, and the resin
treated with KCl gave 7 g. 4-methyl-3-pyrazolyl(thioacetomorpholide)-HCl
(X), m. 202° (decomps.); (from alc.). X (7 g.) hydrolyzed as above
gave 0.22 g. 4-methylpyrazolyl-3-acetic acid, m. 216-17° (from
CCHl3); in the pea curvature test all the acids were inactive at concns.
up to 500 p.p.m.
IT 10237-56-8P, Pyrazole-5-carboxylic acid, 3-acetyl-1,4-dimethyl-
10656-77-1P, Pyrazole-3-acetic acid, 5-carboxy-1,4-dimethyl-
112511-68-8P, Pyrazole-3-acetic acid, 5-carboxy-1,4-dimethyl-,
3-methyl ester 123186-99-5P, Pyrazole-3(or 5)-acetic acid, 5(or
3)-carboxy-4-methyl-
RL: PREP (Preparation)
(preparation of)
RN 10237-56-8 CAPLUS
CN 1H-Pyrazole-5-carboxylic acid, 3-acetyl-1,4-dimethyl- (CA INDEX NAME)

RN 10684G-77-1 CAPLUS
CN 1H-Pyrazole-3-acetic acid, 5-carboxy-1,4-dimethyl- (CA INDEX NAME)

RN 112511-68-8 CAPLUS
CN 1H-Pyrazole-3-acetic acid, 5-carboxy-1,4-dimethyl-, 3-methyl ester (CA
INDEX NAME)

RN 123186-99-5 CAPLUS
CN 1H-Pyrazole-3-acetic acid, 5-carboxy-4-methyl- (CA INDEX NAME)

L4 ANSWER 131 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1957:1763 CAPLUS
DOCUMENT NUMBER: 51:1763
ORIGINAL REFERENCE NO.: 51:373a,374a-i,375a
TITLE: Chlorination of pyrazoles
AUTHOR(S): Buttel, Rudolf; Schafer, Otto; Welzel, Gerhard
CORPORATE SOURCE: Univ. Munich, Germany
SOURCE: Justus Liebigs Annalen der Chemie (1956), 598, 186-97
CODEN: JLACBF; ISSN: 0075-4617
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Dry Cl was passed into 2.75 g. pyrazole (I) in 50 cc. CCl4 at 0°
giving 88% of an HCl salt which treated with aqueous Na2CO3 gave 55%
4-chloropyrazole (II), m. 76-7° (from petr. ether, after H2O
extraction). Into 3.4 g. I in 95 cc. refluxing CCl4 was passed 60 g. Cl
within
4.5 hrs. The hot filtered mixture evaporated to dryness in vacuo gave
1.95 g.
[crude] 1-(4'-chloro-3'-pyrazolyl)-3or
5'-(4''-chloro-1''-pyrazolyl)-4-dichloropyrazole (III), C9H5N6Cl3, nearly
colorless felted needles, m. 232° (from AcOH containing little H2O,
followed by precipitation from H2O with Me2CO), insol. in 2N NaOH and
nearly
insol. in hot concentrated HCl. III (0.7 g.) refluxed with 9 cc. AcCl
gave the
mono-Ac derivative of III, m. 151-2° (from CCl4), reconverted into III
by refluxing with MeOH. I (2 g.) in 20 cc. H2O with 30 g. Cl at
80° cooled and filtered from II, neutralized with solid Na2CO3,
cooled with ice and filtered, gave 0.3-0.4 g.
1-(1,1,3,3-tetrachloro-3-hydroxypropyl)-4-chloropyrazole (IIIa), m.
119° (from ligroine and CCl4) followed by sublimation at
120°, in vacuo), unchanged by heating at 150°, stable to Br,
KMnO4, and FeCl3, hydrolyzed gradually by boiling H2O. Saponification
with cold
10% NaOH or hot 60% H2SO4 gave II almost quantitatively. II and Ac2O
gave
the 1-Ac derivative of II, with empyreumatic odor, m. 72-4° (from Me2CO
by precipitation with H2O and vacuum sublimation). The 1-(C13OCO)
derivative
monohydrate of II, m. 93-4° (after sublimation in vacuo). I (0.306
g.) in 10 cc. H2O and 5 cc. AcOH with a 9% solution containing 0.338
g. NaOCl
gave 0.22 g. II. I (0.136 g.) in H2O with 0.26 g. glacial AcOH and 0.447
g. NaOCl gave (after H2O extraction) 0.16 g. III. The 3-Me derivative
IV of I
(2.65 g.) in 15 cc. CCl4 treated with a rapid Cl stream at 70° gave
4.1 g. HCl salt of the 5-Cl derivative (V), m. 173-7°, which with
aqueous Na2CO3 gave V, m. 65° (from petr. ether). IV (1.6 g.) in
glacial AcOH at 70° was treated with Cl until the temperature dropped,
giving, after concentration in vacuo, the 5-Cl derivative of V, m.
115-17°
(from H2O after treatment with C). IV (2.85 g.) in 26 cc. glacial AcOH
was treated with 67 g. Cl and after 18 hrs. evaporated to dryness in
vacuo,
giving at 0° a mixture of oil and crystals which yielded 18%
3-trichloromethyl-4,5-dichloropyrazole (VI), m. 166-7° (from petr.
ether, b. 60-90°). Crude VI (1.82 g.) boiled 1 hr. with H2O gave
1.2 g. 5-carboxy analog of VI, m. 240-2° (decomposition) (from H2O).
The 4,5-di-Me derivative of IV (2.2 g.) in 27 cc. glacial AcOH with 25
g. Cl,

L4 ANSWER 131 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN (Continued)
followed by evapn. in vacuo gave 74%
4-methyl-3,5-bis(trichloromethyl)pyrazole, m. 198-206° (from AcOH
or petr. ether or sublimation in vacuo). 4 g. of which boiled with H2O 5
hrs. gave 1.36 g. 3,5-dicarboxy-4-methylpyrazole, decomp. 308°
(from H2O). The 1,5-di-Me deriv. of IV (7.2 g.) in 31 cc. glacial AcOH
treated with a slow stream of Cl at 80°, evapd. to dryness in vacuo
and distd. fractionally, gave 96% 1-methyl-5-trichloromethyl deriv. of V,
oil, with camphor-like odor, b7 112-15°. The corresponding
1-methyl-5-carboxy deriv. of V, m. 225° (decomps.); this heated at
240-60° gave the 1-Me deriv. of V (identified as the HCl salt, m.
143-6°; picrate, m. 104-5°). In AcOH with Cl, the
1,3,4,5-tetra-Me deriv. of I gave 61% (slightly impure)
1,3,4-trimethyl-5-trichloromethylpyrazole, b1.5 88-93°. The
corresponding 5-carboxy analog, m. 179° (decomp.), at
250-60° gave the 1,3,4-tri-Me deriv. of I, whose picrate, m.
164°. 4-Iodo-3,5-dimethylpyrazole (VII) (cf. Morgan and Ackeman,
C.A. 17, 2580) chlorinated gave 1-iodo-4-chloro-3,5-dimethylpyrazolium
chloride (VIIa), 2 g. of which digested with 20 cc. H2O gave 0.9 g.
insol.
3,5-di-Me deriv. of II (picrate, m. 192°). The mother liquors
yielded iodine and small amts. of the 4-iodo deriv. of VII, tan, m.
238-9°, readily reduced by H2SO3 or KI in acid to VII. Bromination
of VII gave 1-iodo-4-bromo-3,5-dimethylpyrazolium bromide, giving with
Na2CO3 small amts. of 1-iodo-4-bromo-3,5-dimethylpyrazole, pale yellow,
n.
222-3° (after darkening at 185°) (after washing with EtOH
and Et2O); this reduced with H2SO3 gave 4-bromo-3,5-dimethylpyrazole. Cl
was passed 0.5 hr. into 1 g. 4-iodopyrazole (VIII) in 30 cc. CCl4, giving
1.19 g. 1-iodo-4-chloropyrazolium chloride, m. 135-40° (decomps.),
also formed from the 4-iodo deriv. (IX) of II, with HCl in Et2O. IX, m.
127-8°, was formed from the HCl salt by addn. of 10% Na2CO3. VIII
(0.45 g.) in 15 cc. CCl4 with 0.27 g. Br in 1 cc. CCl4 gave 0.68 g.
1-iodo-4-bromopyrazolium bromide, m. 135-40°, also formed from
1-iodo-4-bromopyrazole, m. 127-8°, and HBr in CHCl3-CCl4. The 4-Br
deriv. of I in CCl4 with Cl gave mainly the HCl salt of II and very small
amts. of III. 4-Nitropyrazole (0.565 g.) in 30 cc. H2O with 0.3 g. AcOH
and 0.375 g. NaOCl gave 0.55 g. colorless 1-chloro-4-nitropyrazole (X),
n.
104-6° (decomps.), decomps. when heated in org. solvents. At
0°, 77 mg. X was added to 50 mg. 3,4-dimethylpyrazole in 0.5 cc.
CCl4, giving 10 mg. trisi(3,4-dimethylhydropyrazole), m. 275-6°
(cf. Buttel, et al., C.A. 50, 9384). Ultraviolet absorption spectra in
EtOH are given for II, IIIa, the hydrate of the 1-ClZC deriv. of II, and
the 1-Oc deriv. of II.
IT 98199-65-3P, Pyrazole-5-carboxylic acid, 4-chloro-1,3-dimethyl-
99968-85-1P, Pyrazole-3,5-dicarboxylic acid, 4-methyl-
115294-67-2P, Pyrazole-5-carboxylic acid, 1,3,4-trimethyl-
RL: PREP (Preparation)
(preparation of)
RN 98199-65-3 CAPLUS
CN 1H-Pyrazole-5-carboxylic acid, 4-chloro-1,3-dimethyl- (CA INDEX NAME)

L4 ANSWER 131 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN (Continued)

RN 99968-85-1 CAPLUS
CN 1H-Pyrazole-3,5-dicarboxylic acid, 4-methyl- (CA INDEX NAME)

RN 115294-67-2 CAPLUS
CN 1H-Pyrazole-3-carboxylic acid, 1,3,4-trimethyl- (CA INDEX NAME)

L4 ANSWER 132 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1954:48705 CAPLUS
DOCUMENT NUMBER: 50:48705
ORIGINAL REFERENCE NO.: 50:9305f-i,9306a-c
TITLE: vic-Dioxoindolyl acid derivatives of pyrazole, isoxazole, and pyrimidine
AUTHOR(S): Jones, R. G.; Whitehead, C. W.
CORPORATE SOURCE: Lilly Research Labs., Indianapolis, IN
SOURCE: Journal of Organic Chemistry (1955), 20, 1342-7
CODEN: JOCRAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 50:48705
AB Adding dropwise 11 g. N2H4.H2O to 48.6 g. EtO2CCOC(:CHCEt)CO2Et (I) in 100 cc. absolute EtOH at 0°, evaporating the solution in vacuo on a steam bath, extracting the residue with Et2O, and distilling the residue of the Et2O extract gives 85% di-Et 3,4-pyrazoledicarboxylate (II), b0.5 160-5°, m. 100-5°, n. 69-70°. Adding 24.3 g. I to 11 g. N2H4.2HCl in 50 cc. H2O and 50 cc. EtOH and heating the mixture on a steam bath 3 hrs. gives 82% 4-carbethoxy-3-pyrazolecarboxylic acid, m. 282° (decomposition). Heating 1 g. II in 25 cc. 6N HCl 4 hrs. on a steam bath gives 3,4-pyrazoledicarboxylic acid (III), m. above 360°. When II is saponified with NaOH and the solution acidified, III sepd. as a clear gel which melts on heating. I with PhNHNH2 or its HCl salt gives 80-4% di-Et 1-phenyl-4,5-pyrazoledicarboxylate (IV), b0.7 160-7°, m2?1 1.5396, saponified with NaOH to the free acid, platelets, m. 214-15°. Adding 42 g. IV in 100 cc. EtOH to 6.5 g. LiAlH4 in 400 cc. Et2O and acetylating the reduction product with Ac2O gives 1-phenyl-4,5-bis(acetoxymethyl)pyrazole, b0.1 170-3°. Treating 42.5 g. II with 500 cc. absolute EtOH saturated with HCl 4 days at 20° gives 85% Et 3-carbethoxy-4-pyrazolecarboxylate, m. 248-50°. Treating IV similarly with NH3-EtOH several months gives 73% unchanged IV. Heating 14.5 g. PhNHNH2.HCl in 100 cc. H2O and 50 cc. EtOH with 21.6 g. EtO2CC(OEt):CCOCOEt:CCOCOEt 15 min. on a steam bath, evaporating the mixture in vacuo to about 100 cc., adding 100 cc. H2O, extracting with Et2O, evaporating the Et2O extract to 150 cc., and adding 150 cc. petr. ether gives 2.1 g. precipitate; adding another 150 cc. petr. ether to the filtered solution yields 53% tri-Et 1-phenyl-3,4,5-pyrazoletricarboxylate, m. 74-4.5° (free acid, m. 213-14°). Adding 24.4 g. I to 8 g. H2NOH.HCl in 50 cc. H2O and 50 cc. EtOH with stirring, then 9 g. NaHCO3, distilling the EtOH in vacuo, adding H2O, and extracting with Et2O gives 66% di-Et 4,5-isoxazoledicarboxylate, b1

L4 ANSWER 132 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN (Continued)

RN 193763-49-4 CAPLUS
CN 1H-Pyrazole-3,4,5-tricarboxylic acid, 1-phenyl- (CA INDEX NAME)

L4 ANSWER 133 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1955:20040 CAPLUS
DOCUMENT NUMBER: 49:20040
ORIGINAL REFERENCE NO.: 49:3948d-i,3949a
TITLE: Heterocyclic syntheses with propargyl alcohol and butynediol. II
AUTHOR(S): Magnani, Elso; Grunanger, Paolo
SOURCE: Atti accad. nazl. Lincei, Rend., Classe sci. fis., mat. e nat. (1953), 14, 275-80
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. C.A. 48, 2684i. The action of PhNH2 on HC.tplbond.CCH2OH (I) gives 2 products, m. 113° and 82°. The compound m. 113° was indicated to be 1-phenyl-4-(hydroxymethyl)-1,2,3-triazole (Ia); Bz derivative, colorless needles, m. 115-16° (MeOH). Alkaline KMnO4 oxidation of Ia gave a white precipitate of 1-phenyl-1,2,3-triazole-4-carboxylic acid (II), needles (H2O), m. 149-50°; CH2N2 gave the Me ester, flakes, m. 120-1° (Et2O). Heating II above its m.p. and cooling the melt solidified on cooling and gave a product, m. 55-6° (H2O), probably 1-phenyltriazole. The substance m. 82°, does not crystallize well from H2O, and is oxidized to 1-phenyl-1,2,3-triazole-5-carboxylic acid, m. 176° (decomposition); Me ester, long soft colorless needles, m. 101-2° (from MeOH). NICH2CO2Et and I gave 78% Et 3-(hydroxymethyl)pyrazole-5-carboxylate acid, small needles (MeOEt), m. 93°. The same reaction in Et2O (instead of MeOH) gave only 21% yield. 3-(Hydroxymethyl)pyrazole-5-carboxylic acid is obtained from the Et ester through the Cu salt, which is dissolved in HCl, precipitated by H2S, and the acid crystallized from H2O, m. 210-12°. The ester and excess NH3 gave the amide, white prismatic crystals, m. 180-1°. Saponification of the amide gave the acid, identical with that obtained from saponification of the ester (mixed m.p.). Oxidation of the free acid by KMnO4 in the cold gave an acid substance crystallizing from H2O in small needles, m. 283°. I and PhCHN2 gave 3-phenyl-5-isoxazolemethanol, m. 82°, colorless flakes, easily soluble in EtOH, Et2O and CS2; Bz derivative, small needles, m. 74-75°. CrO3 in the cold gave the corresponding aldehyde, needles from H2O, m. 119-90°; the n.p. and other properties correspond to those of 3-phenyl-5-isoxazolecarboxylic acid. PhNH2 and butynediol (III) gave 77% white prismatic crystals, m. 161-2°, of 1-phenyl-4,5-di(hydroxymethyl)-1,2,3-triazole (IV); Bz derivative, long colorless prisms, m. 91-2° (from MeOH). Alkaline KMnO4 and IV gave the dicarboxylic acid, small needles, m. 147-8° (decomposition); (from H2O). Methylation with CH2N2 gave di-Me 1-phenyl-1,2,3-triazole-4,5-dicarboxylate, colorless needles from MeOH, m. 126-7°. Alkaline oxidation of IV gave 1-phenyl-4-(hydroxymethyl)-1,2,3-triazole-5-carboxylic acid, small needles from EtOH, m. 173° (decomposition); 1-Phenyl-4-(hydroxymethyl)-1,2,3-triazole, small needles from H2O, m. 112-13° was formed by decarboxylation of the preceding acid; KMnO4 oxidation gave 1-phenyl-1,2,3-triazole-4-carboxylic acid, m. 149-50° (decomposition), which upon decarboxylation gave 1-phenyltriazole, m. 55°. HC.tplbond.CCH and NI gave 37% Et 3,4-di(hydroxymethyl)pyrazole-5-carboxylic acid (V), m. 145-5.5° (MeOH), 145.5° (AcOEt), white needles, soluble in H2O, alc., and

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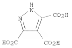
insol. in Et2O. V with KMnO4 gave the acid, obtained as the tri-K salt, silky needles from cold H2O; acidification with conc. HCl gave the free acid, needles, m. 228° (decompn.); CH2N2 gave the Me ester, colorless needles, m. 117-18°.

IT 19551-66-7, 3,4,5-Pyrazoletricarboxylic acid
(and derivs.)

RN 19551-66-7 CAPLUS

CN 1H-Pyrazole-3,4,5-tricarboxylic acid (CA INDEX NAME)



L4 ANSWER 134 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1954:28744 CAPLUS
DOCUMENT NUMBER: 48:28744
ORIGINAL REFERENCE NO.: 48:5173d-i,5174a-i,5175a-b
TITLE: Constitution of usnic acid
AUTHOR(S): Barton, D. H. R.; Bruun, T.
CORPORATE SOURCE: Birkbeck Coll., London
SOURCE: Journal of the Chemical Society (1953) 603-9
CODEN: JCSOA9; ISSN: 0368-1769
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

GI For diagram(s), see printed CA Issue.

AB Evidence in support of the usnic acid (I) formula of Curd and Robertson (C.A. 31, 6219.6) is presented. From (+)-I were prepared the (+)-diacetate [(+)-II], m. 203-4° (from MeOH), [α]D 240° (c, 2.85), λmaximum 224 mμ (ε 26000) and inflections at 249 and 305 mμ (ε 17000 and 9000, resp.); (+)-anhydrophenylhydrazone [(+)-III], m. 199-200° (from CHCl3-EtOH), [α]D 620° (c 2.13, CHCl3) and 624° (c 1.40), λmaximum 221, 253, 287, and 370 mμ (ε 37000, 29000, 24000, and 4000, resp.); and (+)-anhydrophenylhydrazone diacetate [(+)-IV], m. 225-6° (from MeOH-CHCl3), [α]D 426° (c 2.15, CHCl3), λmaximum 245 and 296 mμ, λinflection 349 mμ (ε 34500, 12500, and 4000, resp.), unchanged on refluxing 4 h. in xylene. Similarly, (-)-I gave (-)-II, m. 203-4°, [α]D -235° (c 1.82, CHCl3); (-)-III, m. 198-9°, [α]D -604° (c 2.28, CHCl3); and (-)-IV, m. 222-3°, [α]D -414° (c 2.12, CHCl3). Attempted oximation of the residual ketonic O of (+)-usnic acid phenylhydrazone anhydrophenylhydrazone (V), m. 235-6° (decomposition) (from EtOH), [α]D 512° (c 2.10, CHCl3), λmaximum 258, 303, and 333 mμ (ε 33000, 24000, and 25500, resp.), or of (+)-IV by heating 1 h. with excess NH2OH.HCl in pyridine failed, the product being (+)-usnic acid anhydrophenylhydrazone oxime, m. 279-80° (decomposition) (from CHCl3), [α]D 610° (c 0.48, CHCl3), λmaximum 223, 257, and 368 mμ (ε 34500, 33500, and 3500, resp.). The unsatd. ketone group in V was indicated by the intense IR band at 1673 cm.-1 (CHCl3). Degradation of 200 mg. (+)- and (-)-III with 10 mL. MeOH and 20 g. KOH 3 h. on the steam bath, dilution with H2O, Et2O extraction, evaporation, and crystallization from CHCl3-petr. ether gave the compds. [(+)-VI], m. 206-7°, [α]D 376° (c 0.72, CHCl3), λmaximum 261 and 326 mμ (ε 18000 and 2000, resp.), and [(-)-VI], C23H22O5N2, m. 206-7°, [α]D -380° (c 0.81), λmaximum 261 and 326 mμ (ε 19500 and 2000, resp.). (+)-VI and (-)-VI coupled readily with diazotized o-H2NC6H4CO2H. (-)-VI gave a diacetate (VII), m. 209-10° (from CHCl3-MeOH), [α]D -280° (c 2.25, CHCl3), λmaximum 262 mμ (ε 17000), but was recovered unchanged on heating 15 h. with NH2OH.HCl in pyridine. Treatment with O3 left VII unchanged. More vigorous degradation of 200 mg. (+)- or (-)-III by heating 1 h. under N with 7.5 g. KOH and 10 mL. H2O, diluting with H2O, acidifying with dilute H2SO4, filtering to remove 126 mg.

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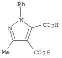
III, extg. the filtrate with Et2O, and extg. the Et2O soln. with 1% and 2% aq. Na2CO3 gave 30 mg. acid (VIII), C22H20O5N2, m. 306° (decompn.) (from CHCl3-MeOH), [α]D0°, λmax. 246, 305, and 352 mμ (ε 26500, 12500, and 4000, resp.) on acidification, while 38 mg. III was recovered from the Et2O; VIII (150 mg.) was obtained by refluxing 200 mg. III 2 h. with 2.5 g. KOH in 10 mL. EtOH. VIII coupled readily with diazotized o-H2NC6H4CO2H. Treatment of VIII with Ac2O-pyridine and then with CH2N2 gave the diacetate Me ester, m. 157-8° (from MeOH or Me2CO), [α]D 0°, λmax. 237 mμ and λinflection 278 and 306 mμ (ε 30000, 8000, and 5000, resp.). Ozonolysis of 500 mg. (+)- or (-)-IV in 20 mL. CCl4 at 0°, decompn. of the ozonide by addn. of EtOH or H2O and heating 15 min. or adding H2O and letting stand overnight, treatment with 1% aq. NaHCO3, and extn. of the CCl4 layer gave 250 mg. neutral tetra-AcO dilactone, which, chromatographed on Al2O3 (washed with EtOAc) and eluted with C6H6, gave pure compd. (IX, R = R' = Ac), m. 225-6° (from CHCl3-MeOH), [α]D 0°, λmax. 220 and 296 mμ (ε 19000 and 2500, resp.), hydrolyzed by cold concd. H2SO4 to the tetra-HO dilactone (IX, R = R' = H), m. 270-1° (decompn.) (from Me2CO), λmax. 240, 286, and 326 mμ (ε 12000, 16000, and 3400, resp.), which on reacetylation gave IX (R = R' = Ac). Et2O extn. of the acidified NaHCO3 solns. gave the acid fraction which in MeOH with a concd. soln. of KOH in MeOH pptd. the K salt, from which acidification liberated 3-methyl-1-phenyl-4,5-pyrazoledicarboxylic acid (X), m. 199-200° (decompn.) (from EtOH-CHCl3 or EtOH-C6H6), λmax. 255 mμ (ε 13000), pK1 2.83, pK2 5.89. On heating X was decarboxylated to 3-methyl-1-phenyl-1-pyrazole-4-carboxylic acid, m. 194-5°, λmax. 266 mμ (ε 21500), pK 4.58. IX (R = R' = Ac) was also obtained by oxidn. of 2 g. (+)- or (-)-II in 100 mL. Me2CO with KMnO4. IX (R = R' = Ac) with MeOH-HCl gave the di-AcO dilactone (IX, R = H, R' = Ac), m. 194-5° (from CHCl3-MeOH), λmax. 220, 256, and 336 mμ (ε 13000, 12500, and 3200, resp.). Ozonolysis of 500 mg. II in 20 mL. CCl4 at 0° produced 4,6-diacetoxy-7-acetyl-3,5-dimethylcoumaran-2-one (XI), m. 1301°, λmax. 218 and 297 mμ (ε 23000 and 3300, resp.), IR bands at 1822, 1780, and 1698 cm.-1, hydrolyzed with cold concd. H2SO4 to 7-acetyl-4,6-dihydroxy-3,5-dimethylcoumaran-2-one, m. 233-4°, λmax. 238, 284, and 332 mμ (ε 12000, 18000, and 3300, resp.). Ozonolysis of XI 1 h. at room temp. or oxidn. with Me2CO-KMnO4 produced IX (R = R' = Ac). Hydrogenation of (+)- and (-)-II gave (+)-dihydrousnic acid diacetate [(+)-XII], m. 148-9° (from MeOH), [α]D 4.5° (c 4.68, CHCl3), λmax. 220, 276, and 316 mμ and λinflection 239 mμ (ε 29000, 11000, 6100, and 18000, resp.), and (-)-XII, m. 148-9°, [α]D -6° (c 4.88, 4.64, and 1.00, CHCl3), resp., with IR bands (CS2) at 1780, 1690, and 1676 cm.-1; hydrolysis with cold concd. H2SO4 produced (-)-dihydrousnic acid, m. 147-8°, [α]D -88° (c 2.86), λmax. 228, 283, and 336 mμ (ε 19000, 25500, and 3600, resp.) and the (+)-isomer, m. 147-8°, [α]D 83° (c 2.38), λmax. 228, 283, and 336 mμ (ε 22000, 26500, and 3900, resp.), resp. XII was recovered unchanged on attempted ozonolysis and on refluxing 6 h. in xylene. The presence of a resacetophenone (XIII) system and hence a C6H6 ring in I was noted on comparison of the UV absorption spectra of III and V with those of XIII and its phenylhydrazone, m. 161-2°, λmax. 246, 304, and 337 mμ

L4 ANSWER 134 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN (Continued)
(ε 15500, 13000, and 25500, resp.) Resacetophenone diacetate (XIV), m. 38-8.5°, λmax. 248 mμ (ε 13500), and the 4-acetate, m. 74-5°, λmax. 257 and 318 mμ (ε 12000 and 4600), were prepd.; IV showed an IR band at 1783 cm.-1 corresponding in intensity to 2 phenolic acetate chromophores, while XIV similarly showed bands at 1760 and 1775 cm.-1 Phloracetophenone overnight at room temp. with Ac2O-pyridine yielded the triacetate, m. 58-9° (from CHCl3-petr. ether), λmax. 239 mμ (ε 6500), giving no color with FeCl3 and unchanged on 30 min. treatment with Me2CO-KMnO4.

IT 25672-12-2P, 4,5-Pyrazoledicarboxylic acid, 3-methyl-1-phenyl-
RL: PREP (Preparation)
(preparation of)

RN 25672-12-2 CAPLUS

CN 1H-Pyrazole-4,5-dicarboxylic acid, 3-methyl-1-phenyl- (CA INDEX NAME)



L4 ANSWER 135 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1948:36531 CAPLUS
DOCUMENT NUMBER: 42:36531
ORIGINAL REFERENCE NO.: 42:7761f-i,7762a-i,7763a-d
TITLE: The Hofmann reaction applied to some pyrazolecarboxamides. I
AUTHOR(S): Musante, Carlo
CORPORATE SOURCE: Univ. Firenze, Italy
SOURCE: Gazzetta Chimica Italiana (1948), 78, 178-91
CODEN: GCITA9; ISSN: 0016-5603
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
GI For diagram(s), see printed CA Issue.
AB The action of KBrO (I) on 5 pyrazolecarboxamides by the classic Hofmann reaction was studied with a view to obtaining the corresponding amines, which either have not been prepared before or have been difficult to prepare
Only amides substituted in the 4-position react normally, with formation of the corresponding amines. On the other hand, with amides in which the 4-position is free, I acts merely as a brominating agent, leaving the CONH2 group unaltered, and forming 4-Br carboxamides. With a large excess
of I, amino-4-bromopyrazoles are obtained in some cases, i.e., bromination
takes place in the 4-position, and the CONH2 group is simultaneously transformed into the NH2 group. Some new derivs. of pyrazole were prepared
in the course of the investigation. Br (0.6 cc.), added dropwise to 1.46 g. HN.N:CMe.CH:CCONH2 (II) (cf. C.A. 41, 4144i) in cold aqueous KOH (1.2 g. in
8.5 cc.), poured into aqueous KOH (1.9 g. in 4 cc.) (the solution turns dark
red), allowed to stand 12 hrs., extracted with Et2O, the alkaline solution acidified
with H2SO4, and the precipitate purified by water and then EtOH, yields 3-methyl-4-bromo-5-pyrazolecarboxamide (III), m. 264° (decomposition). Its solns. in 20% aqueous NaOH are yellow, and when boiled evolve NH3; the
resulting solution, acidified with H2SO4, and the precipitate purified from water,
yield HN.N:CMe.CBr:CCO2H (IV), m. 258-9° (decomposition) (cf. Auwers and Cauer, C.A. 24, 3508). It is prepared also by heating 3.78 g. HN.N:CMe.CH:CCO2H (cf. Ann. 279, 217(1894)) in 200 cc. glacial AcOH on a steam bath, cooling, adding 1.5 cc. Br, allowing to stand, dissolving the precipitate in aqueous Na2CO3, precipitating by HCl, and purifying by water and EtOH. This
anomalous behavior of II with I in comparison with the behavior of aromatic derivs. can be explained electronically on the basis of 2 mesomers of the pyrazole anion, which render the 4-position of the nucleus
readily attacked by cationoid substituents. IV (1.7 g.) and 5 g. SOCl2, refluxed 8 hrs., Et2O added, and the precipitate washed with Et2O, purified by
PhNO2, and washed with Et2O, yield N.N:CMe.CBr:C.CO.N.N:CMe.CBr:C.CO (V) (no m.p. given). With excess concentrated NH4OH, it forms a yellow substance

L4 ANSWER 135 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN (Continued)
which changes gradually into a white substance. This, allowed to stand several hrs., filtered, and the residue washed with water, yields the amide, C5H6ON3Br, of V, m. 265-7°. Recrystd. from hot EtOH, it m. 270°. III (0.75 g.) gives a rose-colored soln. in aq. KOH (6 g. in 15 cc.), which, treated with 0.2 cc. Br, allowed to stand several hrs., filtered, the filtrate concd. in vacuo over H2SO4, the ppt. (probably a K salt) dissolved in water, acidified with dil. H2SO4, and the ppt. purified
by EtOH, yields HN.N:CMe.CBr:CNH2 (VI), m. 258-9° (cf. C.A. 42, 562b). It is formed also by heating 0.7 g II in aq. KOH (2.5 g. in 10 cc.) and 1.79 g. Br on a steam bath, allowing to stand several hrs., acidifying with dil. H2SO4, and purifying the ppt. by EtOH and animal charcoal. Attempts to prep. VI in still other ways were unsuccessful, e.g., when nitrated, HN.N:CMe.CBr:CH (VII) does not form HN.N:CMe.CBr:CNO2
as the necessary intermediate. Thus a mixt. of 8 cc. H2SO4 (20% SO3) and 8 cc. HNO3 (d. 1.48), added slowly to 2.3 g. VII, allowed to stand several
hrs., poured into ice water, neutralized with Na2CO3, extd. with Et2O, the
ext. dried with Na2SO4, distd., and the residue purified by EtOH, yields HN.N:CMe.C(NO2):CH, m. 133-4° (cf. Knorr, Ann. 279, 229(1884); M., C.A. 42, 913c). This easy substitution of Br by NO2 depends on the polarization of the CBr bond induced by the 2 nuclear N atoms. HN.N:CMe.C(NO2):CCONH2 (cf. C.A. 41, 4144i) (2 g.) in 8.5 cc. 14% KOH, treated slowly with 0.6 cc. Br, poured into 3.8 cc. 50% KOH (yellow ppt. and orange-red mother liquor), heated several min. at 50-70°, allowed to stand, dild. with water, and the ppt. purified by EtOH, yields HN.N:CMe.C(NO2):CNH2, m. 226° (cf. C.A. 38, 4597.3). HN.N:CH.CH:CCONH2 (cf. C.A. 41, 4144i; 42, 913c) (0.5 g.), several cc. dil. KOH, and 5 g. Br, allowed to stand, and the ppt. purified by water, yield 4-bromo-5-pyrazolecarboxamide (VIII), m. 220°. Boiled several min., VIII and 10% NaOH evolve NH3, and, acidified with dil. HCl, they ppt. 4-bromo-5-pyrazolecarboxylic acid (IX), m. 240° (decompn.), sol. in dil. Na2CO3 (repptd. by acids). KMnO4 (10.57 g.), added slowly to boiling aq. HN.N:CH.CBr:CMe [cf. Ann. 279, 227(1894)] (5.28 g. in 500 cc.), refluxed several hrs., filtered, concd., acidified with H2SO4, the ppt. dissolved in aq. Na2CO3, repptd. by HCl, and purified
by water, yields IX. The m.p. of IX varies a little with the rate of heating. H2NCON.N:CMe.CH:CMe [Ber. 34, 3973(1901)] (1 g.), added slowly to ice-cold I (from 1.15 g. Br in 6 cc. 25% KOH), heated on a steam bath until an oil forms, allowed to stand ice-cold, and the cryst. product purified by water yields HN.N:CMe.CBr:CMe (X), m. 117° (cf. Morgan and Ackermann, C.A. 17, 2580). Treated with satd. picric acid, and the ppt. purified by EtOH, it forms a picrate, C5H7N2Br.C6H3O7N3, lustrous yellow, m. 197°. KMnO4 (3.2 g.), added slowly to boiling aq. X (0.78 g. in 50 cc.), the filtered soln. concd., acidified with dil. H2SO4,
and the ppt. purified by water, yields HN.N:C(CO2H).CBr:CCO2H.3H2O (XI), m. 274° [cf. Knorr, Ber. 28, 715(1894), who mentions XI, but does not give its prepn. or phys. and chem. properties]. It loses its 3H2O mols. at 110°, and at 290-300° undergoes decarboxylation. The product, taken up in hot water, clarified with animal charcoal, and

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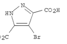
purified by water, yields HN.N:CH.CBr:CH, m. 96-8°. Also HN.N:C(CO2H).CH:CCO2H [cf. Gazz. chim. ital. 22, ii, 359(1892)] (2.5 g.) in 100 cc. water, treated with 0.8 cc. Br, and the ppt. purified by water,
yields XI. Application, as in the present work, of the Hofmann reaction to pyrazolic amides shows several general facts: (1) when the amide contains a free 4-position, I introduces Br in this position and leaves the CONH2 group unaltered, (2) when I is in excess, the CONH2 group is transformed into the NH2 group, with formation in every case of the corresponding amine brominated in the 4-position, and (3) whenever the amide has its 4-position occupied by a substituent, e.g., NO2, I forms directly the corresponding amine.
IT 1085717-89-0P
RL: SPN (Synthetic preparation); PRP (Properties); PREP (Preparation)
(The Hofmann reaction applied to some pyrazolecarboxamides. I)
RN 1085717-89-0 CAPLUS
CN 1H-Pyrazole-3,5-dicarboxylic acid, 4-bromo-, hydrate (1:3) (CA INDEX NAME)



● 3 H2O

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ACCESSION NUMBER: 1948:2604 CAPLUS
DOCUMENT NUMBER: 42:2604
ORIGINAL REFERENCE NO.: 42:562a-i,563a-i,564a-g
TITLE: The Curtius degradation applied to some pyrazolecarboxylic acids
AUTHOR(S): Musante, Carlo; Mugnaini, Elso
CORPORATE SOURCE: Univ. Firenze, Italy
SOURCE: Gazzetta Chimica Italiana (1947), 77, 182-98
CODEN: GCITA9; ISSN: 0016-5603
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
GI For diagram(s), see printed CA Issue.
AB The most interesting product from the reaction of β-nitroisoxazoles with hydrazines, which involves the conversion of the isoxazole nucleus to
the pyrazole nucleus, is 3-methyl-4-nitro-5-aminopyrazole (I) (cf. C.A. 38, 4597.3; 41, 1223i, 4143i, 7298e). In the present work it is shown that I can be prepared in a different way, viz., from 3-methyl-4-nitro-5-pyrazolecarboxylic acid (II) (cf. C.A. 41, 4144i) by the Curtius degradation reaction. The same reaction was also applied to other acid derivs. of pyrazole. Among other findings, it is shown that the hydrazides of these acids are formed by the action of hydrazines on the corresponding diketopiperazinic derivs., with opening of the central piperazinic ring, and that by the action of NH2OH the corresponding hydroxamic acids are formed by an analogous mechanism. In this work numerous new derivs. of pyrazolic acids were prepared, including hydrazides,
azides, urethans, and amines. The Et ester (2.4 g.) of II and 4 cc. H2NNH2.H2O, heated 2 hrs. on a steam-bath, EtOH added, filtered, and the yellow residue purified by water or EtOH, yield 83% of the hydrazide, HN.N:CMe.C(NO2):CCONHNH2 (III), of II, m. 189°, reduces NH3-AgNO3. Alc. III and BzH, heated, yield the benzylidene derivative, C12H11O3N5, m.
251°. Cold III (1.83 g.) in 22 cc. N HCl and 0.9 g. aqueous KNO2 give a precipitate which, filtered, washed with water, and dried over H2SO4 in vacuo,
yields 62% of the azide, HN.N:CMe.C(NO2):CCON3 (IV), of III, decompose approx. 80°. IV (1.4 g.) and 6 cc. anhydrous EtOH, refluxed, evaporated to dryness, and the residue purified by EtOH, yield 3-methyl-4-nitro-5-pyrazolylurethan, HN.N:CMe.C(NO2):CNHCO2Et (V), m. 200°. The reaction is: IV + EtOH → V + N2. V (1.2 g.) and 8 cc. concentrated HCl, heated in a sealed tube several hrs. at 120-40°, the yellow-brown solution evaporated to dryness, dissolved in water, almost
neutralized by NaOH, and the precipitate washed with water and purified by EtOH,
yield 0.7.g. (87%) of I, m. 225-6°. The reaction is V + H2O → I + EtOH + CO2. HN.N:CMe.CH:CCO2H (VI) (cf. Ann. 279, 217(1894)) (12.5 g.), 60 cc. anhydrous EtOH, and 1.5 cc. concentrated H2SO4, refluxed 3-4
hrs., evaporated, dissolved in 5 vols. water, neutralized by Na2CO3, allowed
to stand, filtered, the mother liquor extracted with Et2O, and the combined
product purified by water, yield the Et ester (VII), m. 83° (prepared otherwise by Knorr, Ann. 279, 219(1894)). OC.C:CH.CMe:N.NCOC:CH.CMe:N.N (VIII) (cf. C.A. 41, 4144i) (3 g.) and 15 cc. H2NNH2.H2O, allowed to stand

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several hrs. (heat is evolved), evapd. to dryness on a steam bath, allowed to crystallize, and purified by EtOH, yield the hydrazide, HN:CMe.CH:CCONHNH2.H2O, of VII. In vacuo over H2SO4, or at 110°, it forms the anhyd. hydrazide (IX), m. 153-4°, reduces NH3-AgNO3. The reaction is: VIII + 2N2H4 → 2IX. VI (9 g.) and 4.5 cc. H2NNH2.H2O, heated several hrs. on a water bath, and the product purified by EtOH or water, yield 80% VIII. VIII and Ac2O yield the di-Ac deriv., C9H12O3N4, m. 173-4°. Alc. VIII and BzH yield the benzylidene deriv., C12H12ON4, lustrous, m. 237-9°. Anisylidene deriv., C13H12O2N4, m. 258-60°. Cinnamylidene deriv., C14H14ON4, m. 258°. Alc. VIII and acetone, evapd. and the product purified by EtOH, yield the acetone deriv., C8H11ON4, m. 239°. Acetophenone deriv., C13H14ON4, m. 217°. Alc. VIII and xylose (equimol. wts.), allowed to stand several hrs., and the ppt. purified by EtOH, yield the xylose deriv., C10H10O5N4, m. 188-9°. Alc. NH2OH (prepd. from 1.4 g. NH2OH.HCl and 0.46 g. NaOEt) and 1.08 g. VIII, refluxed, allowed to stand several hrs., evapd. on a steam bath, the residue dissolved in water, acidified with AcOH, and the ppt. purified by EtOH, yield 3-methyl-5-pyrazolecarbohydroxamic acid (X), m. 170° (decompn.); with FeCl3 it gives an intense violet-red color. VII (1.54 g.) and Alc. NH2OH (from 1.4 g. NH2OH.HCl and 0.46 g. NaOEt), refluxed, yield X. Aq., KNO2 (4.2 g.), added dropwise to IX (6.9 g.) in 100 cc. N HCl, the ppt. washed with water, and dried over H2SO4 in vacuo, yields 4.7 g. of the azide, HN.N:CMe.CH:CCON3 (XI), m. 112-14° (decompn.). In boiling EtOH or water, it evolves gas, probably N. Likewise in hot water it evolves gas, and, when filtered hot and allowed to crystallize, gives a compd. which is probably bis(3-methyl-5-pyrazolyl)urea, formed from 2 mols. XI and H2O, with elimination of CO2 and N. XI (4.7 g.) and 11 cc. anhyd. EtOH, refluxed 30 min., distd., the residual sirup allowed to crystallize in a desiccator, and the product purified by Et2O contg. a little EtOH, or preferably by water, yield 3-methyl-5-pyrazolylurethan (XII), m. 158°. XII (2.3 g.) and a few cc. of concd. HCl, heated several hrs. in a sealed tube at 120-40° or on a water bath, concd. on a water bath, allowed to crystallize, and purified by water, yield 3-methyl-5-aminopyrazole-HCl, HN.N:CMe.CH:CNH2.HCl.H2O (XIII), loses its H2O when heated at 110°, m. 258°; with AgNO3 its aq. solns. ppt. AgCl. The filtrate from the XIII, made alk. with NaOH (NH3 is evolved), BzCl added in accordance with the Schotten and Baumann reaction, and the ppt. purified by EtOH, yields 1-benzoyl-5-methyl-3-benzamidopyrazole (XIV), BzN.CMe:CH.C(NHBz):N or N:CMe.CH:C(NHBz).NBz, m. 122°. Since NH3 was evolved when the soln. was made alk., it might be assumed that HN.N:CMe.CH:CNH2 (XV), which may have a desmotropic form, HN.N:CMe.CH2.C:NH, can form 3-methyl-5-pyrazolone (XVI) (cf. J. prakt. Chem. 39, 52(1889); Ber. 29, 253(1896)). However, alk. XVI, treated with BzCl, forms, after purification from EtOH, in low yield a di-Bz deriv., BzN.CMe:CH.CBz:N or N:CMe.CH:CBz.NBz, m. 128-9°, which is therefore different from XIV. II (14.2 g.) and 60 g. SnCl2.2H2O in 60 cc. concd. HCl, heated several min. on a steam bath, Sn added, allowed to stand 12 hrs., decanted into 3 l. of hot water, H2S passed through, filtered, concd. in vacuo, allowed to

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stand, and the ppt. purified by water, yield 3-methyl-4-amino-5-pyrazolecarboxylic acid-HCl, H-i N.N:CMe.C(NH2.HCl):CCO2H. (XVII), m. 220° (decompn.). Its m.p depends on the rate of heating; e.g., when heated very slowly it m. 213-14°. Aq. XVII, made alk. by NaOH, and acidified by AcOH, and the ppt. purified by water, yields 3-methyl-4-amino-5-pyrazolecarboxylic acid, m. 208° (decarboxylation). With alk. 2-naphthol it forms a bright red compd. m. 283°. Aq. NaNO2 (0.5 g.), added dropwise to 1 g. XVII in cold dil. HCl, poured into CuCl in boiling concd. HCl (N is evolved), extd. with Et2O, the ext. evapd., the residue dissolved in aq. Na2CO3, the filtered soln. acidified by HCl, and the ppt. purified by water, yields 3-methyl-4-chloro-5-pyrazolecarboxylic acid, m. 259° (cf. von Auwers and Cauer, C.A. 24, 3508). Aq. KNO2 (0.5 g. in 5 cc.), added dropwise to 1 g. XVII in cold dil. HCl (2 cc. concd. HCl dild. to 10 cc.), poured into aq. KBr (3 g. in 40-50 cc.), powd. Cu added (N is evolved), allowed to stand, heated on a steam bath, extd. with Et2O, the ext. dried by Na2SO4, evapd., the residue dissolved in aq. Na2CO3, filtered, acidified with dil. HCl, and the ppt. purified by water, yields 3-methyl-4-bromo-5-pyrazolecarboxylic acid (XVIII), m. 256-7° (cf. von A. and C.). XVIII (6.1 g.), 50 cc. anhyd. EtOH, and 3.5 cc. concd. H2SO4, refluxed 3 hrs., distd., the residue taken up in water, the cryst. mass treated with dil. Na2CO3, and purified by water, yield the Et ester (XIX) of XVIII, m. 103-4° (cf. 105-8° of von A. and C.).

Attempts to brominate XVIII did not give the expected results, e.g., 1.5 g. XVIII in 30 cc. glacial AcOH and 0.6 cc. Br give a ppt. which, purified by EtOH, yields the compd., C7H9O2N2Br, m. 144°, to be investigated later. XIX (9 g.) and alc. H2NNH2.H2O (15 cc. in 15-20 cc.), refluxed 2-3 hrs., concd., filtered, and the residue purified by EtOH and water, yield 3-methyl-4-bromo-5-pyrazolecarboxylic acid hydrazide (XX), lustrous, m. 230-1°, reduces NH3-AgNO3. Alc. XX and BzH, allowed to stand, and the ppt. purified by EtOH, yield the benzylidene deriv., C12H11ON4Br, m. 269-70°. Aq. KNO2 (1.25 g.), added dropwise to 3.18 g. XX in 40 cc. N HCl, filtered, and the residue washed with water and dried in vacuo over H2SO4, yields 2.6 g. 3-methyl-4-bromo-5-pyrazolecarboxylic acid azide (XXI), decomp. 125°. XXI (2.6 g.) and 10 cc. EtOH, refluxed 2 hrs. (gas is evolved), concd., the rose-colored oily residue (which could not be crystd. by prolonged storage in vacuo in a desiccator) taken up in water, filtered, the residue washed, and dried, yield 3-methyl-4-bromo-5-pyrazolylurethan (XXII), could not be crystd., but m. 139-40°. Its N content was higher than the theoretical value, and probably it contained a little of the corresponding urea deriv. XXII (1.85 g.) and 5 cc. concd. HCl, heated in a sealed tube 3 hrs. at 200°, do not form the expected HN.N:CMe.CBr:CNH2 (XXIII), for the brown liquid product evapd., taken up in water, BzCl added, made alk. with NaOH, agitated energetically and allowed to stand, the semisolid treated with cold EtOH, and the solid purified by EtOH, yields XIV. Under milder conditions the reaction is different. XXII (2 g.) and 5 cc. concd. HCl, refluxed 30 min., the excess HCl evapd., taken up in water, evapd., and the ppt. purified by EtOH, yield 3-methyl-4-bromo-5-aminopyrazole (XXIV),

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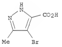
m. 255°. The formation of XIV from XXII is an unusual reaction and not easy to interpret. Possibly XXIII is formed, but if so it then oxidizes the EtOH, formed in the scission of XXI, to AcH, thus: XXIII + EtOH → XV + AcH + HBr. This seems to be confirmed by the fact that when XXII is hydrolyzed by HCl under conditions whereby EtOH is liberated or by a relatively short time of heating, XXIV is formed. The oxidizing action of XXIV is to be studied further. The 2 nuclear N atoms as well as the amino N in the 5-position, by their simple alternating effect, contribute to the polarization of the C-Br bond in such manner as to facilitate the liberation of the Br as a cation.

IT 861382-63-0P
RL: SPN (Synthetic preparation); PRP (Properties); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(The Curtius degradation applied to some pyrazolecarboxylic acids)

RN 861382-63-0 CAPLUS

CN 1H-Pyrazole-5-carboxylic acid, 4-bromo-3-methyl- (CA INDEX NAME)



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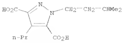
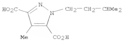
ACCESSION NUMBER: 1944:25003 CAPLUS
DOCUMENT NUMBER: 38:25003
ORIGINAL REFERENCE NO.: 38:3649g-i,3650a-d
TITLE: Pyrazolecarboxamides
AUTHOR(S): Eidebenz, E.; Koulen, K.
SOURCE: Archiv der Pharmazie und Berichte der Deutschen Pharmazeutischen Gesellschaft (1943), 281, 171-85
CODEN: APBDAJ; ISSN: 0376-0367
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB The physiol. effects of 34 amides, dialkylamides and morpholides of N-alkylated 3- or 5-pyrazolecarboxylic and 3,5-dicarboxylic acids were determined In general these were found to be stimulants, hypnotics, analgesics and antipyretics. The procedures for the synthesis of these substances are given. 3-Methyl-5-pyrazolecarboxylic acid morpholide, m. 162°; 1,3-dimethyl-5-pyrazolecarboxylic acid morpholide, m. 75-76°. 3-Methyl-1-isopropyl-5-pyrazolecarboxylic acid, m. 140-141°; Et ester, b23 128-41°; chloride, b11 89°; morpholide, m. 85°. 5-Methyl-1-isopropyl-3-pyrazolecarboxylic acid Et ester, b23 161-163°; chloride, m. 44°; morpholide, m. 52° (0.5 mol. H2O). 5-Methyl-1-allyl-3-pyrazolecarboxylic acid, m. 88°; Et ester, b19 169-73°; chloride, b11 157°; morpholide, m. 92-3°. 3-Methyl-1-allyl-5-pyrazolecarboxylic acid, m. 124°; Et ester, b19 120-32°; chloride, b11 101-102°; morpholide, m. 79-80°. 3,5-Pyrazoledicarbonyl chloride, m. 86-7°; 3,5-pyrazoledicarboxylic anhydride, m. 310°; 3,5-pyrazole-dicarboxylic acid dimorpholide, m. 194-6°. 1-Ethyl-3,5-pyrazoledicarboxylic acid, m. 243°; di-Et ester; dichloride, b12 125°; dimorpholide, m. 123°. 1-Isopropyl-3,5-pyrazoledicarboxylic acid, m. 285°; di-Me ester, m. 66°; dichloride, b17 145-6°; bis(dimethylamide), m. 104-5°; dimorpholide, m. 99.5°; dipiperidide. 1-Allyl-3,5-pyrazoledicarboxylic acid, m. 225°; di-Et ester, m. 39°; dichloride; dimorpholide. 1-Butyl-3,5-pyrazoledicarboxylic acid dimorpholide, m. 126-7°. 1-Isobutyl-3,5-pyrazole-dicarboxylic acid, m. 215°; dichloride, b28 162-4°; dimorpholide, m. 90°. 1-Isoamyl-3,5-pyrazoledicarboxylic acid, m. 243°; di-Et ester, b12 182-6°; dichloride, b20 174-7°; dimorpholide, m. 82°; bis(diethylamide), b3 224-6° (decomposition); bis(dimethylamide); diamide, m 203°; bis(morpholinylethylamide). 1-(Diethylmethyl)-3,5-pyrazoledicarboxylic acid, m. 214°; dichloride; dimorpholide, m. 127°. 1-Hexyl-3,5-pyrazoledicarboxylic acid, m. 189°; di-Et ester; dichloride, b18 183.5-4.5°; dimorpholide, m. 79°. 1-Benzyl-3,5-pyrazoledicarboxytic acid dimorpholide, m. 139-40°. 1-(Phenylethyl)-3,5-pyrazoledicarboxylic acid, m. 224°; dichloride, m. 86°; dimorpholide, m. 110°; 1-Phenacyl-3,5-pyrazoledicarboxylic acid di-Et ester, m. 128°; dimorpholide. 1-Isoamyl-4-methyl-3,5-pyrazoledicarboxylic acid, m 233°; dichloride, b16 176°; diamide, m. 203°; dimorpholide, m. 69-73°. 1-Hexyl-4-methyl-3,5-pyrazoledicarboxylic acid dimorpholide, m. 100°. 1-Isoamyl-4-propyl-3,5-pyrazoledicarboxylic acid, m. 169°; dichloride, b5 160-3°; dimorpholide, m. 74-5°. 1-Ethyl-4,5-pyrazoledicarboxylic acid, with 1 mol. H2O, m. 179-80°; di-Me ester, b20 204-7°; dichloride; dimorpholide, m. 84°. 1-Isoamyl-3,4,5-pyrazoletricarboxylic acid, m. 177°; tri-Me ester,

L4 ANSWER 137 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN (Continued)
m. 47°; trimorpholide, m. 145°.
IT 854699-67-5P, 3,5-Pyrazoledicarboxylic acid, 1-isoamyl-4-propyl-
854699-70-0P, 3,5-Pyrazoledicarboxylic acid, 1-isoamyl-4-methyl-
RL: PREP (Preparation)
(preparation of)
RN 854699-67-5 CAPLUS
CN 1H-Pyrazole-3,5-dicarboxylic acid, 1-(3-methylbutyl)-4-propyl- (CA INDEX NAME)

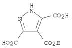


RN 854699-70-0 CAPLUS
CN 1H-Pyrazole-3,5-dicarboxylic acid, 4-methyl-1-(3-methylbutyl)- (CA INDEX NAME)



L4 ANSWER 138 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1944:11782 CAPLUS
DOCUMENT NUMBER: 38:11782
ORIGINAL REFERENCE NO.: 38:1742f-i,1743a-c
TITLE: Synthesis of diazole- and triazoledialdehydes
AUTHOR(S): Henkel, Konrad; Weygand, Friedrich
SOURCE: Berichte der Deutschen Chemischen Gesellschaft [Abteilung] B: Abhandlungen (1943), 76B, 812-18
CODEN: BDCBAD; ISSN: 0365-9488
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 38:11782
AB o-C6H4(CHO)2 condenses with glyoxal in the presence of CN ions in faintly alkaline solution, with simultaneous dehydrogenation by atmospheric O, to isonaphthazarin (C. A. 37, 3426.1). To determine whether heterocyclic o-dialdehydes will similarly condense to dihydroxyquinones, it was necessary to prepare such aldehydes, none of which were known. The synthesis of the derivs. of pyrazole and 1,2,3-triazole seemed to offer most promise. [.tplbond.CCH(OEt)2]2 (I), m. 18-19°, was obtained in 205-g. yield by treating the EtMgBr from 70 g. Mg and 320 g. EtBr in 2 l. ether for 24 h. with purified C2H2, decanting off the ether, pouring the residual dark oil into 450 g. HC(OEt)3 in 500 cc. benzene, boiling the resulting magma with stirring for 5 h. and an addnl. 48 h. without stirring, and decomposing with AcONH4 according to Wohl and Mylo, (C. A. 6, 1007). I (26.1 g.) kept 8 days at 20° in the dark in a dry solution of CH2N2 (from 22 g. Me(NO)NCONH2) in 30 cc. ether gave 24.6 g. of the bis(di-Et acetal), b0.01 137-8°, of 4,5-pyrazoledicarboxaldehyde (II), m. 203-5° (decomposition, Berl), obtained in 98% yield from the acetal heated 10 min. on the water bath with 0.5 N H2SO4. I and N2CHCO2Et heated 24 h. at 80° in absolute alc. gave 60% of the bis(di-Et acetal), red oil not distilling up to 130° under 1 mm., decomposing without distilling at about 200°, to 3-carbethoxy-3,4-pyrazoledicarboxaldehyde (III) (65% from the acetal), m. 179-80° (decomposition, Berl), oxidized by KMnO4 in KOH to 3,4,5-pyrazoletricarboxylic acid, m. 213-15°, agreeing in solubility, in its formation of a difficultly soluble mono-K salt and in its crystallization with 2 H2O, with Buchner's acid (Ber. 22, 846(1889)), which he reports as m. 233° (decomposition). 1 - Ph - 1,2,3 - triazole - 4,5-dicarboxaldehyde bis(di-Et acetal) (IV) (28.8 g. from 20 g. I, 11.9 g. PhN3 and 2 cc. alc. heated 28 h. at 100° in a sealed tube), light yellow oil, b0.01 41°, m. 59° (Berl); free dialdehyde (92% yield), b0.01 122°, m. 107° (Kofler), oxidized to the dicarboxylic acid, m. 146-7° (evolution of CO2). 1-Benzyl homolog of IV (78% from PhCH2N3), b0.16 166-7°, forms neither a picrate nor a picrolonate; free dialdehyde (95%), b0.01 120° (air bath), m. 89° (Kofler). Hexyl azide (12 g. from 30 g. C6H13Br (b761 156-8°), 15 g. NaN3 (Newman, C. A. 29, 3665.7; com. NaN3 does not react with alkyl halides), 150 cc. MeOH and 200 cc. water heated 6 h. at 90° in a sealed tube with shaking), b758 156-7°, n20D

L4 ANSWER 138 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN (Continued)
1.4325. Hexyl analog of IV (90%), b0.08 145°, n21D 1.4571; dialdehyde (90%), b0.1 104-6°, n19D 1.4960. Dodecyl azide (80%), b2 98°, n19D 1.4552; dodecyl analog of IV (75%), b0.01 184°, n20D 1.4591; dialdehyde (98%), b0.1 168°, m. 30-2.5°. No addn. product of NH3 to I could be obtained, probably because I is cleaved by the acid and the (.tplbond.CCHO)2 is not stable. The above dialdehydes are sol. in 2 N NaOH, insol. (except III) in 2 N Na2CO3, give pos. fuchsin-SO2 and Tollens tests and neg. Legal (II and III, faintly pos.), FeCl3, NH3 + AcOH, and Zimmermann (glycocoll) tests, thus resembling o-C6H4(CHO)2 (except for the last 2 tests and their soly. in 2 N NaOH).
IT 19551-66-7P, 3,4,5-Pyrazoletricarboxylic acid
RL: PREP (Preparation)
(preparation of)
RN 19551-66-7 CAPLUS
CN 1H-Pyrazole-3,4,5-tricarboxylic acid (CA INDEX NAME)



L4 ANSWER 139 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1939:59781 CAPLUS
DOCUMENT NUMBER: 33:59781
ORIGINAL REFERENCE NO.: 33:8610g-i,8611a-d
TITLE: Pyrazole synthesis. VI. Action of α-halo hydrazones on the sodium salts of asymmetric β-diketones
AUTHOR(S): Fusco, Raffaello
SOURCE: Gazzetta Chimica Italiana (1939), 69, 364-78
CODEN: GCITA9; ISSN: 0016-5603
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Although the condensation of the α-halo hydrazone p-O2NC6H4NHN:CBrCO2Et (I) with the asym. β-diketones, BzCH2Ac (II), AcCH2CHO (III), AcCH2COCO2Me (IV) and BzCH2COCO2Me (V), presents the possibility of cyclization in 2 directions, only 1 isomeric form is produced in quantities sufficient for isolation. Condensation of 1 mol. I with 2 mols. of the crude Na salt of III in alc. by boiling for several min., filtration, concentration and recrystn. from alc. gave moderate yields of 1-p-nitrophenyl-3-carbethoxy-4-benzoylpyrazole (VI), m. 165° (p-nitrophenylhydrazone, m. 283°), saponified to the acid (VII), m. 263° (decomposition) (p-nitrophenylhydrazone, m. 300°), which was decarboxylated at 270° to the ketone, 1-p-nitrophenyl-4-benzoylpyrazole, m. 195-7° (p-nitrophenylhydrazone, m. 251°). Similarly condensation of I and II gave 1-p-nitrophenyl-3-carbethoxy-4-benzoyl-5-methylpyrazole (VIII), m. 170°, saponified to the corresponding acid (IX), m. 200° (decomposition), non-reactive with p-O2NC6H4NH:NH2, stable to concentrated HNO3 and giving no CHI8 with KOH and I. Decarboxylation of IX at 200-5° gave 1-p-nitrophenyl-4-benzoyl-5-methylpyrazole, m. 155-6°. Oxidation of IX with alkaline KMnO4 and decarboxylation of the product by boiling in tetralin produced 1-p-nitrophenyl-4-benzoylpyrazole-3-carboxylic acid, m. 263°, identical with VII. Addition of 31 g. I to a mixture of 2.3 g. Na in 15-20 cc. MeOH and 20.6 g. V in 250 cc. of anhydrous benzene and crystallization of the product from alc. Et2O produced 1-p-nitrophenyl-3-carbethoxy-4-benzoyl-5-carbomethoxypyrazole (X), m. 136-8°, saponified to the 3,5-dicarboxylic acid, m. 185-90°, which was decarboxylated to VII. Condensation of I with IV in the presence of MeONa gave 50% yields of 1-p-nitrophenyl-3-carbethoxy-4-acetyl-5-carbomethexypyrazole (XI), m. 158-9°, saponified to the corresponding 3,5-dicarboxylic acid, m. 176° (p-nitrophenylhydrazone, m. 258-61° (decomposition)), oxidized by boiling with HNO3 to 1-p-nitrophenylpyrazole-3,4,5-tricarboxylic acid, and giving Lieben's reaction. Since only 1 isomer is found it is possible to arrange in a "scale of reactivity" the various groups which activate the CO group and enable it to unite with the NH group of the halo hydrazone to form the pyrazole nucleus. This scale: H, CO2R, Me, Ph, may be combined with a previous similar scale obtained in research on the isoxazole group (C. A. 31, 180.3) to form the scale: H, CO2R, Me, Ph, OEt, NH2. The influence of groups in positions 3 and 5 on the reactivity of the group CO in position 4 toward p-O2NC6H4NHNH2 is discussed.
IT 854699-76-6, 3,5-Pyrazoledicarboxylic acid, 4-acetyl-1-(p-nitrophenyl)-

L4 ANSWER 139 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN (Continued)
(and derivs.)
RN 854093-76-6 CAPLUS
CN 1H-Pyrazole-3,5-dicarboxylic acid, 4-acetyl-1-(4-nitrophenyl)- (CA INDEX NAME)

L4 ANSWER 140 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN (Continued)
L4 distd. under 13 mm., it begins to evolve gas at 80° and yields V(1, b13 155-8°; semicarbazone, C15H21O5N3, m. 254°. VII, from VI with H and Pt oxide in AcOEt, b13 148-50°; semicarbazone, m. 218°. VIII, from I slowly added to a suspension of reduced Cu in pyrrole on the water bath, m. 85°. 4-Me deriv., from I and 4-methylpyrrole, m. 106°, immediately decolorizes Br in AcOH, giving the β,β'-di-Br deriv., m. 162°.
α,β'-Di-Me homolog of VIII, from I and 2,4-dimethylpyrrole, m. 114°. X, b14 180-4°, m. 64-6°.
IT 19351-66-7P, 3-Isopyrazole-3,4,5-tricarboxylic acid
RL: PREP (Preparation)
(preparation of)
RN 19351-66-7 CAPLUS
CN 1H-Pyrazole-3,4,5-tricarboxylic acid (CA INDEX NAME)

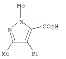
L4 ANSWER 140 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1935:50645 CAPLUS
DOCUMENT NUMBER: 32:50645
ORIGINAL REFERENCE NO.: 32:9208h-i,9209a-f
TITLE: Diene syntheses. XXXI. Behavior of azibutenone toward unsaturated systems
AUTHOR(S): Roels, Otto; Romug, Hans
SOURCE: Berichte der Deutschen Chemischen Gesellschaft [Abteilung] B: Abhandlungen (1935), 71B, 1179-85
CODEN: BCGBAD; ISSN: 0365-9488
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 32:50645
GI For diagram(s), see printed CA issue.
AB It seemed possible that azibutenone (I) (C. A. 9, 1180) might react, with elimination of N, as a philodienic component in diene syntheses. The present paper describes expts. along these lines. I does not react with aliphatic dienes and nonaromatic cyclopentadienes but does with pyrroles. It is surprising, therefore, that it is indifferent toward the condensed pyrroles indole, 4-methylindole and skatole. With (.tplbond.CCO2Et)2 it reacts extremely violently to form di-Et 3-methyl-3-acetylpyrazole-4,5-dicarboxylate (II) which is saponified, with loss of the Ac group, to 3-methylpyrazole-4,5-dicarboxylic acid (III). This on oxidation yields pyrazole-3,4,5-tricarboxylic acid (IV). I also reacts readily with the active bicyclohexyl-ene double bond of dicyclopentadiene, first forming an adduct (V) still containing the 2 N atoms which, however, are eliminated on vacuum distillation; in the resulting compound (VI) the presence of the CO group can readily be detected, and hydrogenation of the double bond gives the saturated ketone (VII). With pyrrole and its homologs, I reacts like diazo esters and ketones (Buchtaeurs and Solomatin, C. A. 26, 138). That, after cleavage of the N, the :CMeCOMe residue couples with the pyrrole nucleus in the rearranged form Me2C:CO was shown by the fact that the product obtained from pyrrole is identical with α-isobutyrylpyrrole (VIII), prepared from pyrrole, EtI, Mg and Me2CHCOCl. With (:NCO2Et)2, with which, if precautions are not taken, it reacts with terrific violence, I gives a labile tetrazoline, AcCMe.N(CO2Et):N.CH(CO2Et):NiN (IX) which loses N and stabilizes itself as di-Et methylacetylhydrazimethazedicarboxylate (X). II, from (.tplbond.CCO2Et)2 in ether slowly treated under a reflux with I so that the ether just comes to a boil, b13 160-1°; di-Me ester, m. 65°; I g. II refluxed 0.5 hr. with 2 N KOH gives 0.5 g. of a mono-Et ester, m. 213° (loss of CO2), of III; refluxing 2 hrs. in a saturated solution of KOH in MeOH, on the other hand, completely saponifies it to III, crystals with 1 H2O, m. 239° (decomposition). IV (2 g. from 2.5 g. III in boiling Na2CO3 slowly treated with aqueous KMnO4), m. 234°, identical with the acid obtained from (:NCO2Et)2 and (.tplbond.CCO2Et)2; tri-Me ester, m. 100°. Heated with lime at 240-50°, IV gives pyrazole. V, oil; semicarbazone, C15H21ON5, m. 218°. When V
IT 19351-66-7P, 3-Isopyrazole-3,4,5-tricarboxylic acid
RL: PREP (Preparation)
(preparation of)
RN 19351-66-7 CAPLUS
CN 1H-Pyrazole-3,4,5-tricarboxylic acid (CA INDEX NAME)

L4 ANSWER 141 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1926:23013 CAPLUS
DOCUMENT NUMBER: 20:23013
ORIGINAL REFERENCE NO.: 20:2856h-i,2857a-c
TITLE: Rosenmund's aldehyde synthesis in a heterocyclic system
AUTHOR(S): Rojahn, C. A.; Fuhling, H. E.
SOURCE: Archiv der Pharmazie und Berichte der Deutschen Pharmazeutischen Gesellschaft (1926), 264, 337-67
CODEN: APBAJ; ISSN: 0376-0367
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB During a study of 1-methylpyrazole-3-, -4- and -5-aldehydes the following compds. were prepared and characterized. It 1,3,5-trimethylpyrazole-4-carboxylate, by the action of MeI or Me2SO4 on Et 3,5-dimethylpyrazole-4-carboxylate, or by condensation of Et diacetoacetate on MeNHNH2, m. 37°, yields with alc. KOH the corresponding acid, m. 211°, which on heating with CO2 and forms 1,3,5-trimethylpyrazole (picrate, C12H13O7N8, m. 144-5°); 2,3,5-trimethylpyrazole-4-carboxylyl chloride, b12 140-50°, m. 67-8° (amide, m. 200°; anilide, m. 159°). Attempts to convert the above acid chloride into the corresponding aldehyde by the aid of BaSO4-Pd catalyst yielded mainly the anhydride, C16H18O3N4, m. 143°, and only very small amts. of 1,3,5-trimethylpyrazole-4-aldehyde (semicarbazone, m. 213-14°), and 1,3,4,5-tetramethylpyrazole (picrate, m. 176-8°). Anhydride of 3(5)-methylpyrazole-5-(3)carboxylic acid, m. 346°, 3(5)-methyl-4-bromopyrazole-5(3)-carboxylic acid, m. 253°, 1,5-dimethylpyrazole-3-carboxylylchloride, b13 120-5°, m. 60° (amide, 177-8°); 1,5-dimethylpyrazole-3-aldehyde, b13 113-20°, m. 56° (semicarbazone, m. 201°; oxime, m. 177-8°; aminoguanidine nitrate, m. 200°). 1,3-Dimethylpyrazole-5-carboxylyl chloride, b12 75-80° (amide, m. 165°); 1,3-dimethylpyrazole-5-aldehyde, b12 80-2° (picrate, m. 133°, semicarbazone, m. 206°, oxime, m. 148°, aminoguanidene nitrate, C7H13ON7, m. 159°). Anhydride of 4-methylpyrazole-3(5)-carboxylic acid, m. 320°. 1,4-Dimethylpyrazole-3-carboxylyl chloride, b20 90-5°, m. 40° (amide, m. 164°, anilide, m. 127°); 1,4-dimethylpyrazole-3-aldehyde, m. 126-7° (semicarbazone, m. 216°, aminoguanidene nitrate, m. 158°). Picrate of 1,4-dimethylpyrazole, m. 165° (methiodide of the base, C6H12N2I, m. 187°. 1,4-Dimethylpyrazole-5-carboxylyl chloride, m. 73-4° (amide, m. 158-60°; anilide, m. 94°).
IT 861382-63-0P, 5-Pyrazolecarboxylic acid, 4-bromo-3-methyl-
RL: PREP (Preparation)
(preparation of)
RN 861382-63-0 CAPLUS
CN 1H-Pyrazole-5-carboxylic acid, 4-bromo-3-methyl- (CA INDEX NAME)

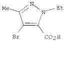
L4 ANSWER 141 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN (Continued)

L4 ANSWER 142 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1926:20419 CAPLUS
DOCUMENT NUMBER: 20:20419
ORIGINAL REFERENCE NO.: 20:2493i,2494a-f
TITLE: Isomerism relationships in the pyrazole series. VI. Alkyl derivatives of 3,5-methylpyrazolecarboxylic acid and of 3(5)-methylpyrazole
AUTHOR(S): v. Auwers, K.; Hollmann, H.
SOURCE: Berichte der Deutschen Chemischen Gesellschaft [Abteilung] B: Abhandlungen (1926), 59B, 601-7
CODEN: BDCBAD; ISSN: 0365-9488
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. C. A. 19, 2953. Alkylation of 3(5)-methylpyrazole (I) by different methods had been found to yield always only 1 kind of dialkylpyrazoles which, on the basis of a series of synthetic expts., had been considered as being the 1,3-derivs., the 1,5-derivs. appearing either not to be formed under the given conditions or to rearrange immediately into the 1,3-isomers. On the other hand, of the alkyl derivs. of 3,5-methylchloropyrazole, those in which the 2 alkyl groups are adjacent are characterized by their special stability whereas the 1,3-dialkyl-5-chloropyrazoles, although they are also formed, are less stable. To determine whether other negative substituents would exert a similar influence on the stability relations in the pyrazole ring the alkylation of Et 3,5-methylpyrazolecarboxylate (II), among other compds., was studied. The results were quite unexpected and necessitated a repetition of some of the results obtained by v. K. and H. are now reported in connection with R. (cf. preceding abstract). When II is boiled in absolute alc. with NaOEt and EtI there are formed 2 isomeric Et N-ethylmethylpyrazolecarboxylates, b12 101.5-2.0° (III) and 154° (IV), the yield of IV being regularly 2-3 times greater than that of III. The corresponding free acids (V and VI), m. 141-2° and 136-7° and at higher temps. yield 2 different N-ethylmethylpyrazoles (VII and VIII), b. 152° and 161° (picrates, m. 114-5° and 143°, resp.). The 4-Br derivs. (IX and X) of V and VI, m. 159° and 149°; with 3% HCl in hot MeOH only X gives a Me ester (XI), m. 65-6°, IX remaining entirely unchanged. It follows, therefore that X has only 1, while IX has 2 substituents adjacent to the CO3H group, and that IV, VI VIII, X and XI are the 1-ethy-5-methyl derivs. and III, V, VII and IX the 1,3-isomers. These results were fully confirmed in a 2nd series of expts., in which by methylation of II were finally obtained 2 dimethylpyrazoles, the 1,5-derivative (XII), b. 153° (picrate, m. 172°), proving to be identical with that previously thought to be the 1,3-derivative (XIII), which b. 136° (picrate, lemon-yellow, m. 137°). The discovery that dialkylpyrazoles, even when not further substituted, can exist in both the 1,3- and 1,5-forms removes these compds. from the peculiar position which they hitherto had been thought to occupy, but, as far as can be seen at present, the fact remains that in their formation a shifting of alkyls may occur in certain cases, and the difficulty of determining

L4 ANSWER 142 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN (Continued)
the structure of the individual compds. is greatly increased by the fact that the course of the reaction of hydrazines with unsatd. aldehydes, ketones and their derivs. depends on a multitude of factors and the reactions can often not be interpreted by the aid of analogy so that all the synthetic expts. reported in the earlier work will have to be gone over again and amplified. IV (40 g. from 55 g. II), thick oil of characteristic odor, b. about 285°, d420 1.079, nHe20 1.4922, sol. in concd. HCl and repptd. on diln. III (yield, 15.5 g.) b. about 235°, d420 1.040, nHe20 1.4768, sol. in dil. HCl; picrate, m. 68-9°, can be pptd. from MeOH with H2O but decomps. into its components on attempted recrystn. from C6H5 or ligroin. VI is sol. in concd. HCl but repptd. by H2O. IX,HBr, m. 194°, hydrolyzed to IX by H2O. VIII, d420 0.951, nHe20 1.4741, is identical with the compd. formerly thought to be the 1,3-deriv. and reported as b. 152°. VII, d420 0.936, nHe20 1.4675. Methylation of II with MeI and NaOMe in MeOH gave 2 Me dimethylpyrazolecarboxylates: 1,5- deriv., cryst. powder, b11 144°, m. 71.5-2.5°; 1,3-isomer, thick oil, b11 91°. Free 1,5-acid, m. 175-6°; 4-Br deriv., m. 194-5° and yields a Me ester, m. 79°. 1,3-Acid, m. 207°; 4-Br deriv., m. 232°. 1,5-Dimethyl-4-bromopyrazole, from the Br acid heated a long time in vacuo above its m. p., m. 38.5-9.5° (picrate, greenish light yellow, m. 122-2.5°), also obtained from XII with Br. in AcOH. 1,3-Isomer, mobile oil, b10 75°; picrate, light yellow, m. 116°.
IT 5775-88-2, 5-Pyrazolecarboxylic acid, 4-bromo-1,3-dimethyl-
175276-99-0, 5-Pyrazolecarboxylic acid, 4-bromo-1-ethyl-3-methyl-
(preparation of)
RN 5775-88-2 CAPLUS
CN 1H-Pyrazole-5-carboxylic acid, 4-bromo-1,3-dimethyl- (CA INDEX NAME)



RN 175276-99-0 CAPLUS
CN 1H-Pyrazole-5-carboxylic acid, 4-bromo-1-ethyl-3-methyl- (CA INDEX NAME)



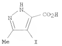
L4 ANSWER 143 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1923:16258 CAPLUS
DOCUMENT NUMBER: 17:16258
ORIGINAL REFERENCE NO.: 17:2580b-g
TITLE: Substitution in the pyrazole series. Halogen derivatives of 3,5-dimethylpyrazole
AUTHOR(S): Morgan, G. T.; Ackerman, Isidore
SOURCE: Journal of the Chemical Society, Transactions (1923), 123, 1308-18
CODEN: JCHTA3; ISSN: 0368-1645
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
GI For diagram(s), see printed CA Issue.
AB The diazo derivs. have been studied as a means of preparing the substitution derivs. of 3,5-dimethylpyrazole (I), but the results showed that the yields were less than by direct halogenation. Iodination occurs much more readily than in the C6H6 series. The 4-NO2 derivative is best prepared by adding 6 cc. HNO3 (d. 1.42) to 10 cc. concentrated H2SO4 containing 5 g. I at 0°, adding 20 cc. additional H2SO4, allowing to stand overnight and then heating 3-4 hrs. at 100°. The reduction to the 4-NH2 derivative is best carried out in moist Et2O with Al-Hg, the yield being 85%. Benzylidene derivative, m. 139-40°; o-Nitrobenzylidene derivative, greenish yellow turning reddish brown on exposure to light and air, m. 101°; m-isomer, light yellow, m. 236°; p-isomer, golden yellow, m. 198°. Aqueous HCHO gives the complex [HOCH2N.N:CMe.C(N:CH2):CMe]x, does not m. 300°. The diazonium chloride condenses with β-diketones and β-keto esters in the presence of aqueous AcONa. 4-Azoacetylacetone derivative, golden yellow, m. 184° (decomposition). 4-Azobenzoylacetone derivative, light yellow, m. 169-70° (decomposition). Et 3,5-dimethylpyrazole-4-azoacetoacetate, orange-yellow, m. 157°. These derivs. gave red Na salts which developed intense red colors with FeCl3. 4-Iodo-3,5-dimethylpyrazole (II), m. 137°, is obtained in 60% yield from boiling aqueous KI and the diazonium chloride, or in quant. yield by heating I, I in KI, AcONa and H2O. Ac derivative, m. 62.5-3.5°. Bz derivative, m. 82°. Chloroaurate, orange-yellow, m. 174°. Chloroplatinate, light orange, m. 215-20°. Dichloride, yellow, m. 85-88°, by passing dry Cl into II in CHCl3; it is very volatile at the ordinary temperature and the vapor is lachrymatory. The action of dilute aqueous NaOH is complicated and destructive and an iodoso derivative could not be isolated. Dibromide, brick-red, m. 78-81°; this also is volatile and lachrymatory. Iodochloride hydrochloride, yellow, m. 111° (decomposition), from ICl.HCl and I in concentrated HCl; it is hydrolyzed by H2O, liberates I from KI and S from aqueous Na2S2O3, 10% NaOH decomps. it quant. into II. Dilute EtOH transforms it into the HCl salt of II, m. 195°. II with alkaline KMnO4 gives 4-iodopyrazolecarboxylic acid, amorphous, decompose above 70°; Ag salt; and 4-iodo-3-(5)-methylpyrazole, m. 185-7°; chloroaurate, orange-yellow; chloroplatinate, orangeyellow. With neutral KMnO4 the

L4 ANSWER 143 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN (Continued)
product is 4-iodo-3-(5)-methylpyrazolecarboxylic acid, amorphous, m. 237°;Ag salt. 4-Bromo-3,5-dimethylpyrazole, m. 118°;chloroaurate, orange-red, m. 126-8°. Ac deriv., m. 38°; Bz deriv., m. 48-9°. Perbromide, by adding Br to I in concd. HCl, orange-red, m. 142-4°. On warming with EtOH, the HBr salt, m. 174°, results. 4-Chloro-3,5-dimethylpyrazole, m. 95°, results by passing Cl into aq. I. It is less basic than the Br or I derivs. and does not yield Ac or Bz derivs. I, warmed with fuming H2SO4 (20% SO3) on the H2O bath for 6 hrs., gives the 4-SO3H acid, contg. 1.5 H2O, m. 287-8°; the H2O is lost at 115°. Chloride, m. 100°.

IT 861553-53-9P, 5-Pyrazolecarboxylic acid, 4-iodo-3-methyl-
RL: PREP (Preparation)
(preparation of)

RN 861553-53-9 CAPLUS

CN 1H-Pyrazole-5-carboxylic acid, 4-iodo-3-methyl- (CA INDEX NAME)



L4 ANSWER 144 OF 145 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1920:7183 CAPLUS
DOCUMENT NUMBER: 14:7183
ORIGINAL REFERENCE NO.: 14:1339h-i,1340a-g
TITLE: Synthesis of thiophene derivatives from β-aminocrotonic ester. II
AUTHOR(S): Benary, Erich; Silberstrom, L.
CORPORATE SOURCE: Univ. Berlin
SOURCE: Berichte der Deutschen Chemischen Gesellschaft [Abteilung] B: Abhandlungen (1919), 52B, 1605-13
CODEN: BDCBAD; ISSN: 0365-9488
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

GI For diagram(s), see printed CA Issue.

AB cf. C. A. 9, 1784. In the earlier paper it was shown that H2NCMe:C(CO2Et)COCH2Cl (A) with KSH (Kahlbaum's 33% solution) gives S.CMe:C(CO2Et).C(OH):CH (B), and on repeating the experiment with pure KSH the same result was obtained, but when the Kahlbaum solution was again used, the reaction took an entirely different course, probably owing to some unidentified impurity in the solution Thus, when 1000 g. A and 250 cc. alc. were treated with 300 cc. of the 33% KSH, the A was converted into a brownish crystalline mass of α-acelylthiotetronamide, H2NCMe:C.CO.S.CH2.CO, long bright yellow needles from alc., m. 233°, soluble in cold acids, gives a red-brown precipitate in alc. with FeCl3, decomposed by boiling N NaOH into NH3 and α-acetyltetronic acid. The alc. mother liquors from the amide contain a little B. The latter is best obtained (75% yield) by adding 25 g. solid KSH to 50 g. A suspended in 150 cc. alc. When 10 g. B in 100 cc. cold AcOH is slowly treated with powdered NaNO2, ethyl 2-nitrimino-3-keto-5-methyl-2,3-dihydrothiophene-4-carboxylate (C), S.CMe:C(CO2Et).CO.C:NNO2, seps. on standing as a yellow-green mass of long needles or as a crystalline powder, decomps. 211°, easily soluble in Na2CO3, repptd. unchanged by acids, reddens litmus, gives the Thiele-Lachmann reaction. With alc. NH3 it forms an addition product, C8H8O5N2S.NH3, orange precipitate, easily soluble in H2O; in this solution Pb(OAc)2 produces a brown-red, Cu(OAc)2 a green precipitate The composition of the lead and silver salts corresponds to that of salts of a dibasic nitri-minic acid, = C:NNO(OH)2; this is also true of the red-brown hygroscopic potassium salt. Similarly, C shaken in concentrated Na2CO3 solution with 3 mols. p-O2NC6H4COCl in a little Et2O gives table-like crystals, m. 162°, of a compound C22H16O12N4S, which may be considered as a diacyl derivative of nitriminic acid, although the possibility of ring opening is not excluded and the compound may have the structure RSCMe:C(CO2Et)COC(OR): NNO2. The free acid of C, from the acid of B and NaNO2 in AcOH, is obtained as a brown precipitate

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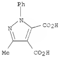
which easily deflagrates; alc. KOH ppts. from its alc. soln. the tribasic potassium salt of the nitriminic acid; the corresponding lead and silver salts explode on heating and in contact with concd. H2SO4. With AmNO2 in alc. instead of NaNO2, the reaction with B stops at the stage of ethyl 2-isonitroso-3-keto-5-methyl-2,5-dihydrothiophene-4-carboxylate (D), yellowish needles from alc., gradually carbonizes 110-30°, gives a red-brown ppt. with FeCl3 in alc., yields C with NaNO2 in AcOH, forms with alc. KOH a dark brown-red K salt sol. in H2O with KMnO4-like color, acids pptg. a bright red substance from the soln. Free acid, similarly obtained from the acid of B, green crystals, decomps. 120-3°, yields a gray-green K salt with alc. KOH. 3-Phenylhydraaone of D, from D and an equal amt. of PhNHNH2 in warm AcOH, long needles from alc., m. 152-3°, easily sol. in Na2CO3 or NH4OH, gives an olive-green color with FeCl3 in alc.; with NaNO2 in AcOH it forms an isomer, pptd. by H2O as a light pink, finely cryst. powder, m. 201°, insol. in Na2CO3 but sol. in NH4OH and alkalies, gives no color with FeCl3 in alc. If the hydrazone is boiled 1 hr. in alc. with a few drops of fuming HCl, it loses S and H2O and is converted into ethyl 1-phenyl-3-methyl-5-cyano-pyrazole-4-carboxylate, needles from alc., m. 88-9°, hydrolyzed on boiling 1.5 hrs. with alc. KOH to the free acid, soft felted needles from AcOH, m. 250-1°; silver salt, white ppt. If the acid is boiled 1 hr. with 6% NaOH it is hydrolyzed to the 4,5-dicarboxylic acid, m. 199-200°.

IT 25672-12-2P, 4,5-Pyrazoledicarboxylic acid, 3-methyl-1-phenyl-
RL: PREP (Preparation)
(preparation of)

RN 25672-12-2 CAPLUS

CN 1H-Pyrazole-4,5-dicarboxylic acid, 3-methyl-1-phenyl- (CA INDEX NAME)



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ACCESSION NUMBER: 1915:10383 CAPLUS
DOCUMENT NUMBER: 9:10383
ORIGINAL REFERENCE NO.: 9:1607d-i,1608a-i,1609a-e
TITLE: Hydrazides and azides of organic acids. XXX. Formation of hydrazihydrazides and hydraziazides of tribasic acids
AUTHOR(S): Curtius, Theodore
CORPORATE SOURCE: Heidelberg
SOURCE: Journal fuer Praktische Chemie (Leipzig) (1915), 91, 39-102
CODEN: JPCEAO; ISSN: 0021-8383
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AB I. With Edmund Bourcart. Tricarballylic acid cannot be converted into C3H5(NH2)3 by the azide method (cf. J. prakt. Chemical 62, 232 (1900)), but tri-Et pyrazoline- 3,4,5-tricarboxylate (a) can be converted into the corresponding tri-NH2 derivative Trimesic, hemimellitic and pyrazoletricarboxylic acids, on the other hand, do not lend themselves to this reaction. Only the sym. tri-CO2H acids form with H4N2.H2O hydrazides and azides of the types (b) and (r), resp., while those having 2 CO2H groups in the o-position form hydrazihydrazides and hydraziazides of the type (I). The instability of 1,3,5-C6H3(NH2)3 probably explains why it cannot thus be obtained from trimesic acid. (a) was prepared by allowing N2CHCO2Et to stand with cold di-Et fumarate; short needles from alc., m. 97°. By adding 10 g. of (a) in 30 g. hot alc. to 10 g. H4N2.H2O in 200 cc. of cold absolute alc., and allowing to stand for 1 hr., pyrazoline-3,4,5-tricarboxyl trihydrazide (b), (R = CONHNH2) R.C:N.NH.CHR.CHR, is formed, white precipitate, cannot be crystallized without decomposition, becomes red 130-40°, m. 148° (decompn). When heated with H2O for 2-3 days, NH3 is evolved, and on cooling a yellow acid seps.; hydrochloride, by adding cold, concentrated HCl to (b), white, hygroscopic precipitate, becomes yellowish red on standing; sulfate and nitrate, both unstable; picrate, small yellow needles; sodium sulfate derivative, white precipitate, becomes red on standing; chloroplatinate; cadmium chloride derivative, white precipitate from (b) + CdCl2; tribensal derivative (R' = PhCH:NNHCO), R'C:N.NH.CHR'.CHR', by shaking (b) in H2O with BzH, white precipitate; tri-p-nitrobenzol derivative, white, light powder; trihydroxybenzal derivative, light yellowish powder, becomes red 130°; trivanillal derivative, light, yellow powder, m. 139° (decomposition); tripiperonal derivative, white precipitate; tricinnamylidene derivative, lemon, microcryst. powder; trifurfural derivative; triacetone derivative; triacetyl derivative, by warming (b) with an excess of Ac2O, white powder, becomes red 100-30°, m. 140° (decomposition); triazide (c), N3OCC:N.NH.CH(CON3).CHCON3, by diazotizing (b) in dilute HCl, and extracting with Et2O, viscous oil, very volatile in vacuo and explodes when heated; trianilide, from (c) in Et2O mid PhNH2, amorphous precipitate from CHCl3, does

not m. below 300°; tri-ptoluide, amorphous ppt. On b. with abs. alc., for 2-3 hrs., (c) was converted into triethyl pyrazoline-3,4,5-tricarbamate, a viscous substance which could not be crystd.; on heating with 3-4 vols. concd. HCl for 24-36 hrs., at 60-70°, until evolution of CO2 had entirely ceased, extg. with alc., filtering off the NH4Cl and concg., a gelatinous residue was obtained whose properties and derivs. showed it to be chiefly pyrazoline-3,4,5-triamine hydrochloride; picrate, short yellow needles from H2O, m. 180° (decompn.). Attempts to obtain the free base in pure form by decompn. of the picrate were unsuccessful. By diazotizing the HCl deriv., adding resorcinol and passing CO2 through the resulting mixt., a dark brown, non-cryst. dye was obtained. Similarly, β-naphthol gave a brown dye. II. With Ludwig H. Heynemann. The tri-Et pyrazole-3,4,5-tricarboxylate (d), used for the following preps., was made from N2CHCO2Et and [C(CO2Et)]2, according to the method of Buchner (cf. Ber. 22, 842). When allowed to stand with NH4OH it gave the triamide, cryst. ppt., decompd. by boiling H2O. (d) was converted into the trihydrazide (e), H2NNHCOC:N.NH.C(CONHNH2):CCONHNH2, by the action of H4N2.H2O in cold. abs. alc., microcryst. powder, does not m. below 300°, sol. in both dil. alks. and acids, and decompd. by boiling with H2O. The following derivs. were prepd. from (e) and the corresponding aldehydes; tribenzal derivative, white, insol. ppt.; trihydroxybenzal derivative, yellow, flocculent ppt.; tri-m-nitrobenzal derivative, yellow ppt.; tricinnamylidene derivative, yellow, microcryst. powder from alc. There was also formed in this reaction cinnamylideneazine, sepd. from the others by Et2O, and the cinnamylidenehydrazihydrazide derivative, insol. in alc. The triazide, N3COC:N.NH.C(CON3).CCON3, prepd. by diazotizing (e), was obtained by slow evapn. from Et2O as a cryst. solid. It explodes on heating, and is completely sapond. by cold dil. Na2CO3; trianilide, rosettes of needles from AcOH, does not m. below 270°. The white residue obtained by boiling the azide in Et2O with abs. alc. for 6 hrs. did not respond to any of the tests for the expected triurethan. When 4 g. of (d) in abs. alc. is boiled for 3-7 hrs. with 2 g. H4N2.H2O, the hydrazihydrazide (I) is obtained in the form of the diammonium salt, needles from H2O; with BzH it gave a benzaldazine derivative, m. 93°; cinnamylidene derivative, m. 162°. (I) was obtained by decompg. the di-NH4 salt with dil. mineral acids. It shows both basic and acidic properties; hydrochloride, prepd. either by addition of concd. HCl or by passing dry HCl into the di-NH4 salt in H2O, white, cryst. powder; heated with dil. H2SO4 only the primary hydrazine residue is removed, while heating with concd. HCl in a closed tube removes the secondary groups with the formation of the diacid ammonium pyrazoletricarboxylate, HO2CC:N.NH.C(CO2H):CCO2N2H6, silky needles, stable at 325°; shaken in H2O with BzH, it yields, together with benzaldazine, the free acid, m. 230° (decompn.); barium salt, white powder. By shaking (I) in H2O with BzH the benzal derivative was obtained as a white, flocculent ppt.; diazotized, (I) yields the hydraziazide (f), yellow, flocculent ppt., which cannot be crsytd., and is easily sapon. by alkalies; heated for 5 hrs. with PhNH2 it

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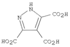
yields the hydrazianilide. On boiling with H2O (f) is converted into pyrazolehydrazicarboxylic acid (II), amorphous powder from H2O, gives a white ppt. with HgCl2 and (AcO)2Pb. Heated with abs. alc., (f) yields a white cryst. powder, becomes brown 220°, and is sol. in strong acids and alkalies. It is probably the hydraziurethan. III With Aloys J. Schmitz. The following derivs. of 1,3,5-C6H3(CO2H)3 were prepd.: Trimesyl trihydrazide (g), C6H3(CONHNH2)3, by boiling for 12-16 hrs. C6H3(CO2Et)3 in abs. alc. with 8 g. H4N2.H2O, microscopic crystals, does not m. below 300;° hydrochloride, by passing HCl into (g) in alc., lustrous needles, unstable in the air, and loses 1 H2O at 100°; tribenzal derivative, C6H3(CONHN:CHPh)3, by direct heating of its components, powder by dissolving in AcOH and pptg. with H2O, m. 224°; triazide, by diazotizing (g) in dil. HCl, white flocculent ppt., explodes on heating or percussion; on boiling for 8 hrs. with H2O, CO2 and N were evolved, but no other product was identified, while on boiling with alc., it yielded triethyl benzenetricarbamate (h), C6H3(NHCO2Et)3, white ppt. dissolving in alc. and pptg. with H2O, m. 110-1°; trianilide, by heating the triazide with PhNH2, brown ppt. from dil. AcOH, m. 118-20° (decompn.). On heating (h) in alc. for 8 hrs. with dil. HCl at 100°, the expected C6H3(NH2)3 was not formed, but a compd. whose analysis agreed fairly closely with that of the aminodiurethan, H2NC6H3(NHCO2Et)2, long needles by pptg. from alc. with H2O, m. 172-3°. The following derivs. of 1,2,3-C6H3(CO2H)3 were prepd.: C6H3(CO2Et)3 from acenaphthene according to the method of Graebe (cf. Ber. 25, 652; 26, 1797; Ann. 290, 206, 217); on heating in alc. with H4N2.H2O it yielded quant. hemimellithylhydrazihydrazide (III), yellow powder, m. above 300°, gives ppts. with CuSO4, AgNO3, HgCl2 and FeCl3; benzal derivative, microcryst. powder, m. above 300°; hydraziazide, white powder; hydrazianilide, yellow, cryst. powder; urethan derivative, white cryst. powder; urea derivative, by heating the hydraziazide with H2O, monoclinic crystals from H2O. Yield, 40%. Heated for 2 hrs. in a closed tube with concd. HCl, it was converted into o-aminophthalyl hydrazide. The latter on heating with concd. HCl for 30-40 hrs. at 145-50° loses 1 mol. H4N2 salt, forming 1,2,3-H2NC6H3-CO2H, which is further converted into m-H2NC6H4CO2H by loss of CO2.

IT 19551-66-7, 3,4,5-Pyrazoletricarboxylic acid
(and derivs.)

RN 19551-66-7 CAPLUS

CN 1H-Pyrazole-3,4,5-tricarboxylic acid (CA INDEX NAME)



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